

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent No.: 5,254,556

Issued: October 19, 1993

Expiration Date: October 27, 2009

Inventors: Cornelus G. M. Janssen, Alfonsus G. Knaeps, Ludo E. J. Kennis, Jan Vandenberg

Title: 3-PIPERIDINYL-1,2-BENZISOXAZOLES

Mail Stop Patent Extension
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

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PATENT EXTENSION
OPLA

**TRANSMITTAL OF APPLICATION FOR INTERIM EXTENSION OF PATENT TERM
(37 C.F.R. § 1.790)**

Attached hereto is an Application for Interim Extension of Patent Term for the above-identified Patent along with (5) copies. In such Petition, Applicant provides the following sections and exhibits.

I. SIGNATURE REQUIREMENTS (37 C.F.R. §1.730)

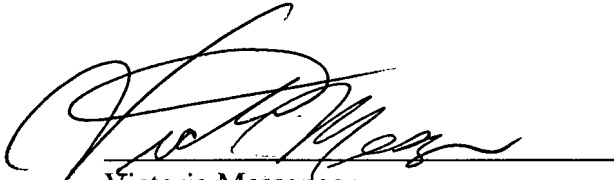
- A. IDENTIFICATION OF PERSON(S) SUBMITTING THE APPLICATION**
- B. RECORDAL OF ASSIGNMENT IN PTO**

II. APPLICATION REQUIREMENTS (37 C.F.R. §§1.790 and 1.740)

- A. IDENTIFICATION OF PRODUCT UNDERGOING REGULATORY REVIEW (1.740(a)(1))**
- B. IDENTIFICATION OF THE FEDERAL STATUTE UNDER WHICH REGULATORY REVIEW IS CURRENTLY TAKING PLACE (1.740(a)(2))**
- C. IDENTIFICATION OF ACTIVE INGREDIENTS AND PREVIOUS APPROVAL INFORMATION (1.740(a)(4))**
- D. IDENTIFICATION OF PATENT (1.740(a)(6), (7), (8))**
- E. IDENTIFICATION OF CLAIMS READING ON THE PRODUCT SEEKING APPROVAL (1.740(a)(9))**
- F. RELEVANT DATES AND INFORMATION (1.740(a)(10))**
- G. DESCRIPTION OF SIGNIFICANT ACTIVITIES OF APPLICANT DURING REGULATORY REVIEW (1.740(a)(11))**
- H. STATEMENT THAT PATENT IS ELIGIBLE FOR EXTENSION (1.740(a)(12))**

- I. ACKNOWLEDGEMENT OF DUTY OF DISCLOSURE (1.740(a)(13))
- J. FEE (1.740(a)(14))
- K. CORRESPONDENCE
- L. COPIES (§ MPEP 2753 (8th Edition, Rev. No. 7))

<u>Exhibit 1</u>	<u>Copy of Merger Documents</u>
<u>Exhibit 2</u>	<u>Copy of U.S. Patent No. 5,254,556</u>
<u>Exhibit 3</u>	<u>Copy of U.S. Patent & Trademark Office Maintenance Fee Statement for U.S. Patent No. 5,254,556</u>
<u>Exhibit 4</u>	<u>Copy of Terminal Disclaimer filed in U.S. Patent No. 5,254,556</u>
<u>Exhibit 5</u>	<u>Claims 1, 2 and 3 of U.S. Patent No. 5254,556 Read on the Active Ingredient of the Product Seeking Approval or its Method of Use</u>
<u>Exhibit 6</u>	<u>Description of Significant Activities of Applicant during Regulatory Review</u>



Victoria Messenger
(703) 330-6011
Schellin & Associates, Ltd.
1940 Duke Street
Suite 200
Arlington, VA 22202

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent No.: 5,254,556

Issued: October 19, 1993

Expiration Date: October 27, 2009

Inventors: Cornelus G. M. Janssen, Alfonsus G. Knaeps, Ludo E. J. Kennis, Jan Vandenberg

Title: 3-PIPERIDINYL-1,2-BENZISOXAZOLES

Mail Stop Patent Extension
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

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APPLICATION FOR INTERIM EXTENSION OF PATENT TERM (37 C.F.R. § 1.790)

Pursuant to 35 U.S.C. § 156(d) and 37 C.F.R. § 1.790, Ortho-McNeil-Janssen Pharmaceuticals, Inc. ("Applicant") as Assignee and patent owner of the above-captioned patent, hereby petitions for an interim extension of U.S. Patent No. 5,254,556 (the '556 Patent). In support of such Petition, Applicant provides the following information:

I. SIGNATURE REQUIREMENTS (37 C.F.R. § 1.730)

A. IDENTIFICATION OF PERSON(S) SUBMITTING THE APPLICATION

I, Hal Brent Woodrow, represent that I am a registered patent practitioner signing on behalf of the patent owner.

B. RECORDAL OF ASSIGNMENT IN PTO

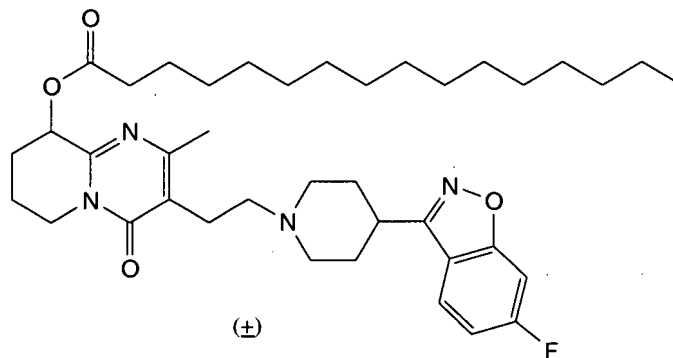
This application, U.S.S.N. 07/932,142, filed August 19, 1992, which is a Divisional of U.S.S.N. 07/422,847, filed October 17, 1989, now issued as US Patent No. 5,158,952, which is a Continuation-in-Part of U.S.S.N. 07/267,857, filed November 7, 1988, which was abandoned. An assignment of U.S.S.N. 07/422,847 was recorded: Date: November 13, 1989 at Reel/Frame: 05171/0567 847 from the named inventors to Janssen Pharmaceutica, N.V., and an assignment of U.S.S.N. 07/422,847 was recorded: Date: October 4, 2006 at Reel/Frame: 018385/0112 from Janssen Pharmaceutica, N.V. to Janssen L.P; which was dissolved by the Limited Partner, Janssen, Inc., and General Partner Janssen Pharmaceutica Inc., when they merged and subsequently became Ortho-McNeil-Janssen Pharmaceuticals, Inc. were recorded in U.S.S.N. 07/422,847: Date: May 20, 2009 at Reel/Frame: 022708/0352 (copies of the merger documents are attached as Exhibit 1). Additionally to further clarify the record US Patent No. 5,254,556 was specifically assigned to Ortho-McNeil-Janssen Pharmaceuticals, Inc. on July 6th, 2009.

II. APPLICATION REQUIREMENTS (37 C.F.R. §§ 1.790 and 1.740)

A. IDENTIFICATION OF PRODUCT UNDERGOING REGULATORY REVIEW (1.740(a)(1))

The United States Food and Drug Administration ("FDA") is currently reviewing New Drug Application ("NDA") No. 22-264 for INVEGA SUSTENNA™ (paliperidone palmitate). The active ingredient of INVEGA SUSTENNA is paliperidone palmitate. The chemical name for paliperidone palmitate is [(9RS)-3-[2-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]ethyl]-2-methyl-4-oxo-6,7,8,9-tetrahydropyrido[1,2-a]pyrimidin-9-yl] hexadecanoate, also known as C₁₆ alkanolic acid ester of 3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-9-hydroxy-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one.

Paliperidone palmitate has the following structural formula:



B. IDENTIFICATION OF THE FEDERAL STATUTE UNDER WHICH REGULATORY REVIEW IS CURRENTLY TAKING PLACE (1.740(a)(2))

Regulatory review for this product is currently occurring under the Federal Food Drug & Cosmetic Act, §505(b), 21 U.S.C. §355 (new drugs).

C. IDENTIFICATION OF ACTIVE INGREDIENTS AND PREVIOUS APPROVAL INFORMATION (1.740(a)(4))

INVEGA SUSTENNA is a human drug product, the sole active ingredient of which is paliperidone palmitate. Neither paliperidone palmitate, nor any salt or ester thereof, has been previously approved, alone or in combination, for commercial marketing or use under the Food, Drug & Cosmetic Act, the Public Health Service Act, or the Virus-Serum-Toxin Act.

D. IDENTIFICATION OF PATENT (1.740(a)(6), (7), (8))

Name of inventors: Cornelus G. M. Janssen
Alfonsus G. Knaeps
Ludo E. J. Kennis
Jan Vandenberg

Patent No.: 5,254,556

Date of issue: October 19, 1993

Expiration date: October 27, 2009

A copy of the patent, including the entire specification (with claims) and drawings is attached as Exhibit 2.

A copy of the U.S. Patent & Trademark Office Maintenance Fee Statement is attached as Exhibit 3.

A terminal disclaimer pursuant to 37 C.F.R. §1.321(a) was filed in the '556 Patent disclaiming the terminal part of the statutory term of any patent which would extend beyond the expiration date of the full statutory term defined in 35 U.S.C. §§154-156 and 173 of U.S. Patent No. 5,158,952. A copy of the disclaimer is attached as Exhibit 4. The '556 Patent remains commonly owned with U.S. Patent No. 5,158,952.

No certificate of correction or reexamination certificate has issued in the '556 Patent.

E. IDENTIFICATION OF CLAIMS READING ON THE PRODUCT SEEKING APPROVAL (1.740(a)(9))

The '556 Patent claims the active ingredient of the Product currently undergoing regulatory review which is paliperidone palmitate. The '556 Patent includes 6 claims, of which Claims 1 and 2 claim the Product, and Claim 3 claims the use of the Product.

A claim chart that lists each applicable claim of the '556 Patent and demonstrates the manner in which each claim reads on the Product is attached as Exhibit 5.

F. RELEVANT DATES AND INFORMATION (1.740(a)(10))

The '556 Patent claims a human drug.

The effective date of the investigational new drug (IND) application was June 2, 2003 and the IND No. is 67,356.

The new drug application (NDA) was initially submitted on October 26, 2007. The NDA No. is 22-264.

The NDA is currently undergoing regulatory review by the FDA.

**G. DESCRIPTION OF SIGNIFICANT ACTIVITIES OF APPLICANT DURING
REGULATORY REVIEW (1.740(a)(11))**

Attached as Exhibit 6 is a "DESCRIPTION OF SIGNIFICANT ACTIVITIES OF APPLICANT DURING REGULATORY REVIEW (1.740(a)(11))" that provides a description of the significant activities undertaken by the marketing applicant during the applicable regulatory review period with respect to the approved Product and the significant dates applicable to such activities.

H. STATEMENT THAT PATENT IS ELIGIBLE FOR EXTENSION (1.740(a)(12))

To the best of my knowledge, the '556 Patent meets all the eligibility criteria set forth in 37 CFR 1.710 and 1.720 for extension of patent term. It is not possible to determine the length of the extension that will ultimately be claimed since approval has not yet been granted for the product. Applicant expects the regulatory review period to extend past the expiration of the '556 patent, and is therefore requesting an interim extension for a period of one year, pursuant to 37 CFR 1.790(a).

I. ACKNOWLEDGEMENT OF DUTY OF DISCLOSURE (1.740(a)(13))

I, Hal Brent Woodrow, the person signing below, acknowledge the duty to disclose to the Director of the U.S. Patent and Trademark Office and to the Secretary of Health and Human Services any information which is material to the determination of entitlement to the extension which is being sought herein.

J. FEE (1.740(a)(14))

The Application fee due is \$420.00 (37 C.F.R. § 1.740(a)(14) and § 1.20(j)(2).

Authorization is hereby made to charge the amount of \$420.00 to Deposit Account No. 10-0750/JAB0828USDIV/HBW.

Please also charge any additional fees required by this paper or credit any overpayment to Deposit Account No. 10-0750/JAB0828USDIV/HBW.

K. CORRESPONDENCE

Please direct all inquiries and correspondence relating to this application to:

Philip S. Johnson, Esq.
Johnson & Johnson
One Johnson & Johnson Plaza
New Brunswick, NJ 08933

Attn: Hal B. Woodrow
Phone: (732) 524-2976
Facsimile: (732) 524-2808

L. COPIES (§ MPEP 2753 (8th Edition, Rev. No. 7).

Four additional copies of this application are attached, making a total of five copies being submitted.

Date: 6 July 2009

Hal Brent Woodrow

Hal Brent Woodrow
Registration No. 32,501
Johnson & Johnson
One Johnson & Johnson Plaza
New Brunswick, NJ 08933
Tel. No. 732-524-2976
Customer No. 27777

Exhibit 1

Copy of Merger Documents

O:PHILIP S. JOHNSON COMPANY:ONE JOHNSON & JOHNSON PLAZA

**UNITED STATES PATENT AND TRADEMARK OFFICE**UNDER SECRETARY OF COMMERCE FOR INTELLECTUAL PROPERTY AND
DIRECTOR OF THE UNITED STATES PATENT AND TRADEMARK OFFICE

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MAY 20, 2009

PTAS

PHILIP S. JOHNSON
ONE JOHNSON & JOHNSON PLAZA
JOHNSON & JOHNSON
NEW BRUNSWICK, NJ 08933UNITED STATES PATENT AND TRADEMARK OFFICE
NOTICE OF RECORDATION OF ASSIGNMENT DOCUMENTTHE ENCLOSED DOCUMENT HAS BEEN RECORDED BY THE ASSIGNMENT DIVISION OF
THE U.S. PATENT AND TRADEMARK OFFICE. A COMPLETE MICROFILM COPY IS
AVAILABLE AT THE ASSIGNMENT SEARCH ROOM ON THE REEL AND FRAME NUMBER
REFERENCED BELOW.PLEASE REVIEW ALL INFORMATION CONTAINED ON THIS NOTICE. THE
INFORMATION CONTAINED ON THIS RECORDATION NOTICE REFLECTS THE DATA
PRESENT IN THE PATENT AND TRADEMARK ASSIGNMENT SYSTEM. IF YOU SHOULD
FIND ANY ERRORS OR HAVE QUESTIONS CONCERNING THIS NOTICE, YOU MAY
CONTACT THE EMPLOYEE WHOSE NAME APPEARS ON THIS NOTICE AT 571-272-3350.
PLEASE SEND REQUEST FOR CORRECTION TO: U.S. PATENT AND TRADEMARK OFFICE,
MAIL STOP: ASSIGNMENT SERVICES BRANCH, P.O. BOX 1450, ALEXANDRIA, VA 22313.

RECORDATION DATE: 05/20/2009

REEL/FRAME: 022708/0352

NUMBER OF PAGES: 10

BRIEF: MERGER (SEE DOCUMENT FOR DETAILS).
DOCKET NUMBER: JAB0650USA

ASSIGNOR:

JANSSEN, INC. THE LIMITED PARTNER
OF JANSSEN, L.P.

DOC DATE: 12/31/2007

ASSIGNEE:

ORTHO-MCNEIL-JANSSEN
PHARMACEUTICALS, INC.
1125 TRENTON-HARBOURTON ROAD
TITUSVILLE, NEW JERSEY 08560

SERIAL NUMBER: 07422847

FILING DATE: 10/17/1989

PATENT NUMBER: 5158952

ISSUE DATE: 10/27/1992

TITLE: 3-[2-[4-(6-FLUORO-1,2-BENZISOXAZOL-3-YL)-1-PIPERDINYL]ETHYL]-6,7,8,
9 TETRAHYDRO-9-HYDROXY-2-METHYL-4H-PYRIDO [1,2-A] PYRIMIDIN-4-ONE,
COMPOSITONS AND METHOD OF USE

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022708/0352 PAGE 2

ASSIGNMENT SERVICES BRANCH
PUBLIC RECORDS DIVISION

O:PHILIP S. JOHNSON COMPANY:ONE JOHNSON & JOHNSON PLAZA

PATENT ASSIGNMENT

Electronic Version v1.1
Stylesheet Version v1.105/20/2009
500864728

SUBMISSION TYPE:	NEW ASSIGNMENT				
NATURE OF CONVEYANCE:	MERGER				
EFFECTIVE DATE:	12/31/2007				
CONVEYING PARTY DATA					
<table border="1"><thead><tr><th>Name</th><th>Execution Date</th></tr></thead><tbody><tr><td>Janssen, Inc. the Limited Partner of Janssen, L.P.</td><td>12/31/2007</td></tr></tbody></table>		Name	Execution Date	Janssen, Inc. the Limited Partner of Janssen, L.P.	12/31/2007
Name	Execution Date				
Janssen, Inc. the Limited Partner of Janssen, L.P.	12/31/2007				
RECEIVING PARTY DATA					
Name:	Ortho-McNeil-Janssen Pharmaceuticals, Inc.				
Street Address:	1125 Trenton-Harbourton Road				
City:	Titusville				
State/Country:	NEW JERSEY				
Postal Code:	08560				
PROPERTY NUMBERS Total: 1					
<table border="1"><thead><tr><th>Property Type</th><th>Number</th></tr></thead><tbody><tr><td>Patent Number:</td><td>5158952</td></tr></tbody></table>		Property Type	Number	Patent Number:	5158952
Property Type	Number				
Patent Number:	5158952				
CORRESPONDENCE DATA					
Fax Number:	(732)524-2808				
<i>Correspondence will be sent via US Mail when the fax attempt is unsuccessful.</i>					
Phone:	7816747816				
Email:	JNJUSPATENT@CORUS.JNJ.COM				
Correspondent Name:	Philip S. Johnson				
Address Line 1:	One Johnson & Johnson Plaza				
Address Line 2:	Johnson & Johnson				
Address Line 4:	New Brunswick, NEW JERSEY 08933				
ATTORNEY DOCKET NUMBER:	JAB0650USA				
NAME OF SUBMITTER:	Kristin Mele				
Total Attachments: 8 source=Merger Docs for 3542a#page1.tif					

CH \$40.00 5158952

O:PHILIP S. JOHNSON COMPANY:ONE JOHNSON & JOHNSON PLAZA

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PHILIP S. JOHNSON COMPANY:ONE JOHNSON & JOHNSON PLAZA

**UNITED STATES PATENT AND
TRADEMARK OFFICE****Facsimile Transmission**

To: Name: PHILIP S. JOHNSON
Company: ONE JOHNSON & JOHNSON PLAZA
Fax Number: 17325242808
Voice Phone:

From: Name: ASSIGNMENT SERVICES BRANCH
Voice Phone: 571-272-3350

37 C.F.R. 1.6 sets forth the types of correspondence that can be communicated to the Patent and Trademark Office via facsimile transmissions. Applicants are advised to use the certificate of facsimile transmission procedures when submitting a reply to a non-final or final Office action by facsimile (37 CFR 1.8(a)).

Fax Notes:

Pg#	Description
1	Cover Page
2	636.TXT
4	Document 1, Batch 1667777

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MAY 21 2009
J & J PAT. DKT. SECTION

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Date and time of transmission: Wednesday, May 20, 2009 9:48:26 PM
Number of pages including this cover sheet: 05

JANSSEN, L.P.

In accordance with the Limited Partnership Agreement of Janssen, L.P., a New Jersey limited partnership, the undersigned, do hereby approve of the following:

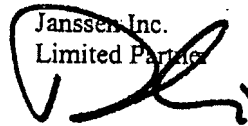
WHEREAS, Janssen Inc. and Janssen Pharmaceutica Inc., are the limited partner and general partner, respectively, of this limited partnership,

WHEREAS, Janssen Inc. wishes to merge with and into Janssen Pharmaceutica Inc., thereby dissolving the limited partnership and filing a certificate of cancellation with the Secretary of State of New Jersey.

NOW, THEREFORE, BE IT RESOLVED, that by virtue of the merger, this limited partnership is hereby dissolved, and further

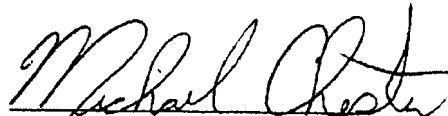
RESOLVED, that a certificate of cancellation be and hereby is filed with the Secretary of State of New Jersey, effective as of December 31, 2007.

Janssen Inc.
Limited Partner



Douglas K. Chia, Vice President

Janssen Pharmaceutica Inc.
General Partner



Michael C. Chester, Secretary

Effective Date: December 30, 2007

LP-103 (10/94)



New Jersey Division of Revenue
Certificate of Cancellation of a Limited Partnership
(Title NJSA 42:2A - 18)

0600071008

1. Name of Limited Partnership:
Jansen, L.P.
2. Limited Partnership Number:
0600071008
3. Date of filing the Certificate of Limited Partnership:
July 1, 1999
4. The Reasons for filing the Certificate of Cancellation are:
The Limited Partnership no longer has assets and is no longer conducting business.
5. The effective date of this Certificate of Cancellation is December 31, 2007.

A Certificate of Cancellation must be signed by all General Partners.

Ortho-McNeil-Janssen Pharmaceuticals, Inc. (General Partner)

Signature [Signature] Date: 12/19/07

Signature James R. Hilton, Vice President Date:

Signature Date:

Signature Date:

Signature Date:

Signature Date:

(If more space is needed, attach an additional sheet)

51945806

J3628712

NJ Division of Revenue, PO Box 308, Trenton, NJ 08625

COMMONWEALTH OF PENNSYLVANIA
DEPARTMENT OF STATE
CORPORATION BUREAU
206 NORTH OFFICE BUILDING
P.O. BOX 8722
HARRISBURG, PA 17105-8722
WWW.CORPORATIONS.STATE.PA.US/CORP

Ortho-McNeil-Janssen Pharmaceuticals, Inc.

THE CORPORATION BUREAU IS HAPPY TO SEND YOU YOUR FILED DOCUMENT. THE CORPORATION BUREAU IS HERE TO SERVE YOU AND WANTS TO THANK YOU FOR DOING BUSINESS IN PENNSYLVANIA.

IF YOU HAVE ANY QUESTIONS PERTAINING TO THE CORPORATION BUREAU, PLEASE VISIT OUR WEB SITE LOCATED AT WWW.CORPORATIONS.STATE.PA.US/CORP OR PLEASE CALL OUR MAIN INFORMATION TELEPHONE NUMBER (717)787-1057. FOR ADDITIONAL INFORMATION REGARDING BUSINESS AND / OR UCC FILINGS, PLEASE VISIT OUR ONLINE "SEARCHABLE DATABASE" LOCATED ON OUR WEB SITE.

ENTITY NUMBER: 681308

CT CORPORATION SYSTEM
100 Pine Street, Suite 325
Harrisburg, PA 17101

Entity #: 681308
Date Filed: 12/18/2007
Effective Date: 12/31/2007
Pedro A. Cortés
Secretary of the Commonwealth

PENNSYLVANIA DEPARTMENT OF STATE
CORPORATION BUREAU

Articles of Amendment-Domestic Corporation
(15 Pa.C.S.)

☒ Business Corporation (§ 1915)
☐ Nonprofit Corporation (§ 5915)

Name			
Address	CT CORP-COUNTER		
City	State	Zip Code	

Document will be returned to the
name and address you enter to
the left.
←

Commonwealth of Pennsylvania
ARTICLES OF AMENDMENT-BUSINESS 3 Page(s)



Fee: \$70

In compliance with the requirements of the applicable provisions (relating to articles of amendment), the undersigned,
desiring to amend its articles, hereby states that:

1. The name of the corporation is:
Janssen Pharmaceuticals Inc.

2. The (a) address of this corporation's current registered office in this Commonwealth or (b) name of its
commercial registered office provider and the county of venue is (the Department is hereby authorized to
correct the following information to conform to the records of the Department):
(a) Number and Street City State Zip County

(b) Name of Commercial Registered Office Provider County
c/o C T Corporation System Alleghany

3. The statute by or under which it was incorporated: Section 1306

4. The date of its incorporation: 12/18/78

5. Check, and if appropriate complete, one of the following:

☐ The amendment shall be effective upon filing these Articles of Amendment in the Department of State.

☒ The amendment shall be effective on: December 31, 2007 at
Date Hour

64411d 813031082

DSCB:15-1915/5915-2

6. Check one of the following:

- ☐ The amendment was adopted by the shareholders or members pursuant to 15 Pa.C.S. § 1914(a) and (b) or § 5914(a).
- ☒ The amendment was adopted by the board of directors pursuant to 15 Pa. C.S. § 1914(c) or § 5914(b).

7. Check, and if appropriate, complete one of the following:

- ☒ The amendment adopted by the corporation, set forth in full, is as follows
That Article I. of the Certificate of Incorporation of this Corporation be amended to read in its entirety as follows:
1. The name of the corporation is: Ortho-McNeil-Janssen Pharmaceuticals, Inc.
- ☐ The amendment adopted by the corporation is set forth in full in Exhibit A attached hereto and made a part hereof.

8. Check if the amendment restates the Articles:

- ☐ The restated Articles of Incorporation supersede the original articles and all amendments thereto.

IN TESTIMONY WHEREOF, the undersigned corporation has caused these Articles of Amendment to be signed by a duly authorized officer thereof this

18th day of December
2007

Janssen Pharmaceuticals Inc.

Name of Corporation

Eric B. Jung
Signature

Eric B. Jung, Vice President

Title

Delaware

PAGE 1

The First State

I, HARRIET SMITH WINDSOR, SECRETARY OF STATE OF THE STATE OF DELAWARE, DO HEREBY CERTIFY THE ATTACHED IS A TRUE AND CORRECT COPY OF THE CERTIFICATE OF MERGER, WHICH MERGES:

"JANSSEN INC.", A DELAWARE CORPORATION,

"MCNEIL NEWCO, INC.", A DELAWARE CORPORATION,

WITH AND INTO "ORTHO-MCNEIL PHARMACEUTICAL, INC." UNDER THE NAME OF "ORTHO-MCNEIL PHARMACEUTICAL, INC.", A CORPORATION ORGANIZED AND EXISTING UNDER THE LAWS OF THE STATE OF PENNSYLVANIA, AS RECEIVED AND FILED IN THIS OFFICE THE TWENTY-FIRST DAY OF DECEMBER, A.D. 2007, AT 9:54 O'CLOCK P.M.

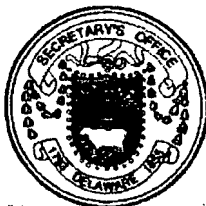
AND I DO HEREBY FURTHER CERTIFY THAT THE EFFECTIVE DATE OF THE AFORESAID CERTIFICATE OF MERGER IS THE THIRTY-FIRST DAY OF DECEMBER, A.D. 2007.

A FILED COPY OF THIS CERTIFICATE HAS BEEN FORWARDED TO THE NEW CASTLE COUNTY RECORDER OF DEEDS.

4479427 8100M

071357631

You may verify this certificate online
at corp.delaware.gov/authver.shtml



Harriet Smith Windsor

Harriet Smith Windsor, Secretary of State

AUTHENTICATION: 6267570

DATE: 12-27-07

State of Delaware
Secretary of State
Division of Corporations
Delivered 10:10 PM 12/21/2007
FILED 09:54 PM 12/21/2007
SRV 071357631 - 2571602 FILE

STATE OF DELAWARE
CERTIFICATE OF MERGER
DOMESTIC CORPORATION INTO
FOREIGN CORPORATION

Pursuant to Title 8, Section 252 of the Delaware General Corporation Law, the undersigned corporation executed the following Certificate of Merger:

FIRST: The name and state of incorporation of each of the constituent corporations to the merger (the "Constituent Corporations") are as follows:

<u>Name</u>	<u>State of Incorporation</u>
Janssen Inc.	Delaware
McNeil Newco, Inc.	Delaware
Ortho-McNeil-Janssen Pharmaceuticals, Inc.	Pennsylvania

SECOND: The Agreement and Plan of Merger has been approved, adopted, certified, executed and acknowledged by each of the constituent corporations pursuant to Title 8, Section 252.

THIRD: The name of the surviving corporation is Ortho-McNeil-Janssen Pharmaceuticals, Inc., a Pennsylvania corporation.

FOURTH: The Certificate of Incorporation of the surviving corporation shall be its Certificate of Incorporation.

FIFTH: The merger is to become effective on December 31, 2007.

SIXTH: The Agreement and Plan of Merger is on file at 1125 Trenton Harbourton Road, Titistville, New Jersey, 08560.

SEVENTH: A copy of the Agreement and Plan of Merger will be furnished by the surviving corporation on request, without cost, to any stockholder of the constituent corporations.

EIGHTH: The surviving corporation agrees that it may be served with process in the State of Delaware in any proceeding for enforcement of any obligation of the surviving corporation arising from this merger, including any suit or other proceeding to enforce the rights of any stockholders as determined in appraisal proceedings pursuant to the provisions of Section 262 of the Delaware General

Corporation laws, and irrevocably appoints the Secretary of State of Delaware as its agent to accept service of process in any such suit or proceeding. The Secretary of State shall mail any such process to the surviving corporation at 1125 Trenton Harbourton Road, Titusville, New Jersey 08560.

IN WITNESS WHEREOF, said surviving corporation has caused this certificate to be signed by its authorized officer, the 19th day of December, 2007.

By: _____

Authorized Officer

Name: James R. Hilton

Title: Vice President



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EFFECTIVE DATE:	12/31/2007										
CONVEYING PARTY DATA											
<table border="1"><thead><tr><th>Name</th><th>Execution Date</th></tr></thead><tbody><tr><td>Janssen, Inc. the Limited Partner of Janssen, L.P.</td><td>12/31/2007</td></tr></tbody></table>	Name	Execution Date	Janssen, Inc. the Limited Partner of Janssen, L.P.	12/31/2007							
Name	Execution Date										
Janssen, Inc. the Limited Partner of Janssen, L.P.	12/31/2007										
RECEIVING PARTY DATA											
<table border="1"><tr><td>Name:</td><td>Ortho-McNeil-Janssen Pharmaceuticals, Inc.</td></tr><tr><td>Street Address:</td><td>1125 Trenton-Harbourton Road</td></tr><tr><td>City:</td><td>Titusville</td></tr><tr><td>State/Country:</td><td>NEW JERSEY</td></tr><tr><td>Postal Code:</td><td>08560</td></tr></table>	Name:	Ortho-McNeil-Janssen Pharmaceuticals, Inc.	Street Address:	1125 Trenton-Harbourton Road	City:	Titusville	State/Country:	NEW JERSEY	Postal Code:	08560	
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PROPERTY NUMBERS Total: 1											
<table border="1"><thead><tr><th>Property Type</th><th>Number</th></tr></thead><tbody><tr><td>Patent Number:</td><td>5158952</td></tr></tbody></table>	Property Type	Number	Patent Number:	5158952							
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CORRESPONDENCE DATA											
Fax Number: (732)524-2808											
Correspondence will be sent via US Mail when the fax attempt is unsuccessful.											
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Total Attachments: 8 source=Merger Docs for 3542a#page1.tif source=Merger Docs for 3542a#page2.tif source=Merger Docs for 3542a#page3.tif source=Merger Docs for 3542a#page4.tif source=Merger Docs for 3542a#page5.tif source=Merger Docs for 3542a#page6.tif source=Merger Docs for 3542a#page7.tif source=Merger Docs for 3542a#page8.tif	
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Exhibit 2

Copy of U.S. Patent No. 5,254,556



US005254556A

United States Patent [19]

Janssen et al.

[11] Patent Number: **5,254,556**[45] Date of Patent: * **Oct. 19, 1993**[54] **3-PIPERIDINYL-1,2-BENZISOXAZOLES**[75] Inventors: **Cornelius G. M. Janssen, Vosselaar; Alfonsus G. Knaeps, Herentals; Ludo E. J. Kennis, Turnhout; Jan Vandenberg, Beerse, all of Belgium**[73] Assignee: **Janssen Pharmaceutica N.V., Beerse, Belgium**

[*] Notice: The portion of the term of this patent subsequent to Oct. 27, 2009 has been disclaimed.

[21] Appl. No.: **932,142**[22] Filed: **Aug. 19, 1992****Related U.S. Application Data**

[60] Division of Ser. No. 422,847, Oct. 17, 1989, Pat. No. 5,158,952, which is a continuation-in-part of Ser. No. 267,857, Nov. 7, 1988, abandoned.

[51] Int. Cl.³ **C07D 487/04; C07D 413/04; A61K 31/505**[52] U.S. Cl. **514/258; 544/282**[58] Field of Search **544/282; 514/258**[56] **References Cited****U.S. PATENT DOCUMENTS**4,804,663 2/1989 Kennis 544/282
5,151,424 9/1992 Janssens 544/282
5,158,952 10/1992 Janssen 544/282*Primary Examiner*—Mark L. Berch*Attorney, Agent, or Firm*—Charles J. Metz[57] **ABSTRACT**

The invention relates to C₂₋₂₀alkanoic acid esters of 3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6, 7,8,9-tetrahydro-9-hydroxy-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one, pharmaceutically acceptable acid addition salts thereof, and enantiomeric forms thereof, which are useful in the treatment of warm-blooded animals suffering from psychotic diseases.

6 Claims, No Drawings

3-PIPERIDINYL-1,2-BENZISOXAZOLES

This application is a division of our copending application Ser. No. 422,847, filed Oct. 17, 1989, now U.S. Pat. No. [5,158,952], which in turn was a continuation-in-part of application Ser. No. 267,857, filed Nov. 7, 1988, now abandoned.

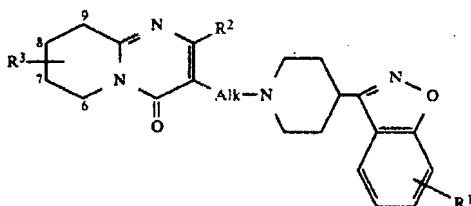
BACKGROUND OF THE INVENTION

In EP-A-0,196,132 there are described a number of 3-piperidinyl-1,2-benzisoxazoles having antipsychotic activity.

The compounds of the present invention differ therefrom by the specific substitution on the (2-C₁₋₄alkyl-6,7,8,9-tetrahydro-4-oxo-4H-pyrido[1,2-a]pyrimidin-3-yl)alkyl substituent at the 1 position of the piperidinyl moiety.

DESCRIPTION OF THE INVENTION

The present invention is concerned with novel 3-piperidinyl-1,2-benzisoxazoles having the formula



the pharmaceutically acceptable acid addition salts thereof, and the stereochemically isomeric forms thereof, wherein

Alk is C₁₋₄alkanediyl;

R¹ is hydrogen, C₁₋₄alkyl or halo;

R² is C₁₋₄alkyl;

R³ is hydroxy or R⁴-C(=O)O-; and

R₄ is C₁₋₁₉alkyl.

In the foregoing definitions C₁₋₄alkanediyl defines bivalent straight and branch chained alkanediyl radicals having from 1 to 4 carbon atoms such as, for example, methylene, 1,2-ethanediyl, 1,3-propanediyl, 1,4-butanediyl and the branched isomers thereof; C₁₋₄alkyl defines straight and branch chained saturated hydrocarbon radicals having from 1 to 4 carbon atoms such as, for example, methyl, ethyl, propyl, 1-methylethyl, butyl, 1-methylpropyl, 2-methylpropyl and 1,1-dimethylethyl; C₁₋₁₉alkyl defines C₁₋₄alkyl radicals as defined hereinabove and the higher homologs thereof having from 5 to 19 carbon atoms such as, for example, pentyl, hexyl, heptyl, octyl, nonyl, decyl, undecyl, dodecyl, tridecyl, tetradecyl, pentadecyl, hexadecyl, heptadecyl, octadecyl, nonadecyl and the like; halo is generic to fluoro, chloro, bromo and iodo. R³ as defined hereinabove may be substituted on any of the 6,7,8 or 9 positions of the 6,7,8,9-tetrahydro-2-C₁₋₄alkyl-4H-pyrido[1,2-a]pyrimidin-4-one moiety.

Particular compounds are those compounds of formula (I) wherein R³ is substituted on the 9 position of the 6,7,8,9-tetrahydro-2-C₁₋₄alkyl-4H-pyrido[1,2-a]pyrimidin-4-one moiety.

More particular compounds within the invention are those particular compounds wherein Alk is ethanediyl;

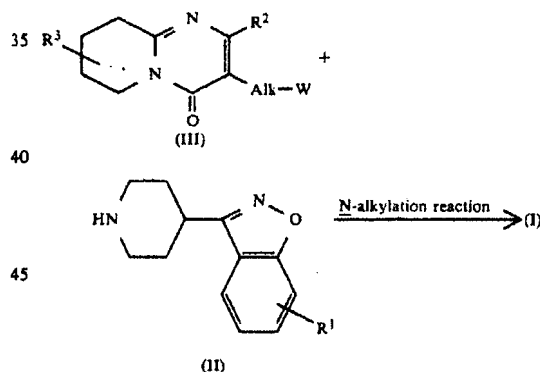
and/or R¹ is halo, in particular fluoro and more in particular 6-fluoro; and/or R² is methyl.

Among the above defined groups of compounds of formula (I) those compounds wherein R⁴ is C₇₋₁₃alkyl, in particular heptyl, nonyl, undecyl or tridecyl are of particular interest.

The most interesting compounds within the invention are selected from the group consisting of 3-[2-(4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl)ethyl]-6,7,8,9-tetrahydro-9-hydroxy-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one, the pharmaceutically acceptable acid addition salt forms and the enantiomeric forms thereof.

From formula (I) it is evident that the compounds of this invention have at least one asymmetric carbon atom in their structure, namely the carbon atom bearing the R³ substituent. The absolute configuration of this centre may be indicated by the stereochemical descriptors R and S, this R and S notation corresponding to the rules described in Pure Appl. Chem. 1976, 45, 11-30. Unless otherwise mentioned or indicated, the chemical designation of compounds denotes the mixture of all possible stereochemically isomeric forms, said mixtures containing all diastereomers and enantiomers of the basic molecular structure. Stereochemically isomeric forms of the compounds of formula (I) are obviously intended to be embraced within the scope of the invention.

The compounds of formula (I) can generally be prepared by N-alkylating a 3-piperidinyl-1,2-benzisoxazole of formula (II) with an alkylating reagent of formula (III) following art-known N-alkylation procedures.



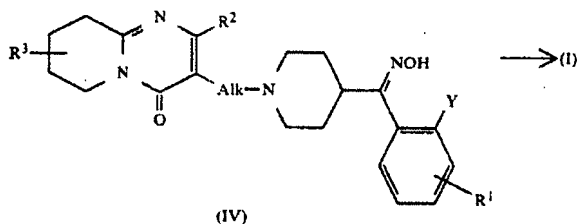
In formula (III) W represents an appropriate reactive leaving group such as, for example, halo, e.g. chloro, bromo or iodo; sulfonyloxy, e.g. methanesulfonyloxy, trifluoromethanesulfonyloxy, benzenesulfonyloxy, 4-methylbenzenesulfonyloxy and the like leaving groups. Said N-alkylation reaction can conveniently be carried out by mixing the reactants, optionally in a reaction-inert solvent such as, for example, water, an aromatic solvent, e.g. benzene, methylbenzene, dimethylbenzene, chlorobenzene, methoxybenzene and the like; a C₁₋₆alkanol, e.g. methanol, ethanol, 1-butanol and the like; a ketone, e.g. 2-propanone, 4-methyl-2-pentanone and the like; an ester, e.g. ethyl acetate, γ-butyrolactone and the like; an ether, e.g. 1,1'-oxybisethane, tetrahydrofuran, 1,4-dioxane and the like; a dipolar aprotic solvent, e.g. N,N-dimethylformamide, N,N-dimethylacetamide, dimethylsulfoxide, pyridine, 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone, 1,3-dimethyl-2-imidazolidi-

none, 1,1,3,3-tetramethylurea, 1-methyl-2-pyrrolidinone, nitrobenzene, acetonitrile and the like; or a mixture of such solvents. The addition of an appropriate base such as, for example, an alkali metal or an earth alkaline metal carbonate, hydrogen carbonate, hydroxide, oxide, carboxylate, alkoxide, hydride or amide, e.g. sodium carbonate, sodium hydrogen carbonate, potassium carbonate, sodium hydroxide, calcium oxide, sodium acetate, sodium methoxide, sodium hydride, sodium amide and the like, or an organic base such as, for example, a tertiary amine, e.g. N,N-diethylethanamine, N-(1-methylethyl)-2-propanamine, 4-ethylmorpholine, 1,4-diazabicyclo[2.2.2]octane, pyridine and the like, may optionally be used to pick up the acid which is formed during the course of the reaction. In some instances the addition of an iodide salt, preferably an alkali metal iodide, or a crown ether, e.g. 1,4,7,10,13,16-hexaoxa-cyclooctadecane and the like, may be appropriate. Stirring and somewhat elevated temperatures may enhance the rate of the reaction; more in particular the reaction may be conducted at the reflux temperature of the reaction mixture. Additionally, it may be advantageous to conduct said N-alkylation under an inert atmosphere such as, for example, oxygen-free argon or nitrogen gas.

Alternatively, said N-alkylation may be carried out by applying art-known conditions of phase transfer catalysis reactions. Said conditions comprise stirring the reactants, with an appropriate base and optionally under an inert atmosphere as defined hereinabove, in the presence of a suitable phase transfer catalyst such as, for example, a trialkylphenylmethylammonium, tetraalkylammonium, tetraalkylphosphonium, tetraarylphosphonium halide, hydroxide, hydrogen sulfate and the like catalysts. Somewhat elevated temperatures may be appropriate to enhance the rate of the reaction.

In this and the following preparations, the reaction products may be isolated from the medium and, if necessary, further purified according to methodologies generally known in the art such as, for example, extraction, crystallization, trituration and chromatography.

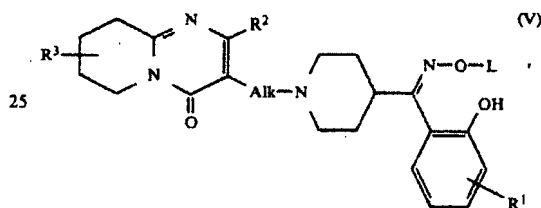
The compounds of formula (I) can also be obtained by the cyclization of an oxime of formula (IV), wherein Y is a reactive leaving group such as, for example, halo or nitro. Preferably Y is a halo group and more particularly fluoro.



Said cyclization reaction of the oxime of formula (IV) may conveniently be conducted by treatment with an appropriate base, preferably in a suitable reaction-inert solvent at temperatures in the range of 20° to 200° C., preferably at 50° to 150° C., and in particular at the reflux temperature of the reaction mixture. Or, if desirable, said base may first be added, preferably at room temperature, whereupon the thus formed oxime salt is cyclized, preferably at an increased temperature and more preferably at the reflux temperature of the reaction mixture. Appropriate bases for said cyclization are,

for example, alkali and earth alkaline metal carbonates, hydrogen carbonates, hydroxides, alkoxides or hydrides, e.g. sodium carbonate, sodium hydrogen carbonate, potassium carbonate, sodium hydroxide, sodium methoxide, sodium hydride or organic bases such as amines, e.g. N,N-diethylethanamine, 4-ethylmorpholine and the like bases. Suitable solvents are, for example, water; aromatic hydrocarbons, e.g. benzene, methylbenzene, dimethylbenzene and the like; halogenated hydrocarbons, e.g. dichloromethane, trichloromethane, 1,2-dichloroethane and the like; lower alkanols, e.g. methanol, ethanol, 1-butanol and the like; ketones, e.g. 2-propanone, 4-methyl-2-pentanone and the like; ethers, e.g. 1,4-dioxane, tetrahydrofuran and the like; dipolar aprotic solvents, e.g. N,N-dimethylformamide, N,N-dimethylacetamide, dimethylsulfoxide, 1-methyl-2-pyrrolidinone and the like, or mixtures of such solvents.

The compounds of formula (I) can also be obtained by cyclizing an activated oxime derivative of formula



wherein L is an acid residue and more particularly is formyl, (C₁₋₆alkyl or aryl)-carbonyl, e.g. acetyl, propionyl, benzoyl and the like; (C₁₋₆alkyl or aryl)oxycarbonyl, e.g. methoxycarbonyl, ethoxycarbonyl, (1,1-dimethyl)ethoxycarbonyl, phenyloxycarbonyl and the like; (C₁₋₆alkyl or aryl)sulfonyl, e.g. methanesulfonyl, benzenesulfonyl, 4-methylbenzenesulfonyl, 2-naphthalenesulfonyl and the like; N-acylaminocarbonyl, e.g. trichloromethylcarbonylaminocarbonyl and the like. Said cyclization reaction of the activated oxime derivative of formula (V) may conveniently be conducted by treatment with an appropriate base, preferably in a suitable reaction-inert solvent, at temperatures in the range from 20° to 200° C., particularly from 50° to 150° C. and preferably at the reflux temperature of the reaction mixture. In some instances however, it may be advanta-

geous not to add a base to the reaction mixture and to remove the acid liberated during the reaction by distillation at normal pressure or, if desired, at reduced pressure. Alternatively, said cyclization may also be effected by heating the oxime derivative (V) in vacuo without a solvent. Appropriate bases are for example, alkali and earth alkaline metal carbonates, hydrogen carbonates and organic amines, e.g. sodium carbonate, potassium carbonate, sodium hydrogen carbonate, N,N-

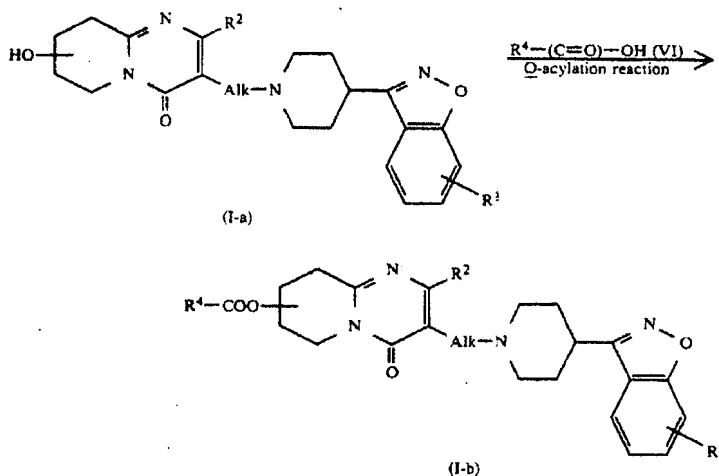
diethylethanamine, 4-ethylmorpholine, 1,4-diazabicyclo[2.2.2]octane, pyridine and the like bases. Suitable solvents for said cyclization are, for example, aromatic hydrocarbons, e.g. benzene, methylbenzene, dimethylbenzene and the like; ethers, e.g. 1,1'-oxybisethane, 1,1'-oxybisbutane, tetrahydrofuran, 1,4-dioxane, 1,1'-oxybis[2-methoxyethane], 2,5,8,11-tetraoxadodecane and the like; dipolar aprotic solvents, e.g. N,N-dimethylformamide, N,N-dimethylacetamide, 1-methyl-2-pyrrolidinone, hexamethylphosphoric triamide, pyridine, acetic anhydride and the like; halogenated hydrocarbons, e.g. trichloromethane, tetrachloromethane, 1,2-dichloroethane, chlorobenzene and the like solvents.

The compounds of formula (I) wherein R^3 is $R^4-(C=O)-O-$, said compounds being represented by formula (I-b), can be obtained by the O-acylation reaction of a compound of formula (I-a) wherein R^3 is hydroxy, with a carboxylic acid of formula (VI) or a suitable reactive functional derivative thereof such as, for example, an acyl halide, symmetric or mixed anhydride, ester or amide, acyl azide and the like derivatives. Said functional derivatives may be prepared following art-known methods, for example, by reacting the carboxylic acid of formula (VI) with a halogenating reagent such as, for example, thionyl chloride, phosphorous trichloride, phosphoryl chloride, oxalyl chloride and the like, or by reacting said carboxylic acid (VI) with an acyl halide such as acetyl chloride and the like. Said derivatives may be generated in situ, or if desired, be isolated and further purified before reacting them with the compound of formula (I-a).

pyridinium iodide, phosphorus pentoxide, 1,1'-carbonylbis[1H-imidazole], 1,1'-sulfonylbis[1H-imidazole] and the like reagents.

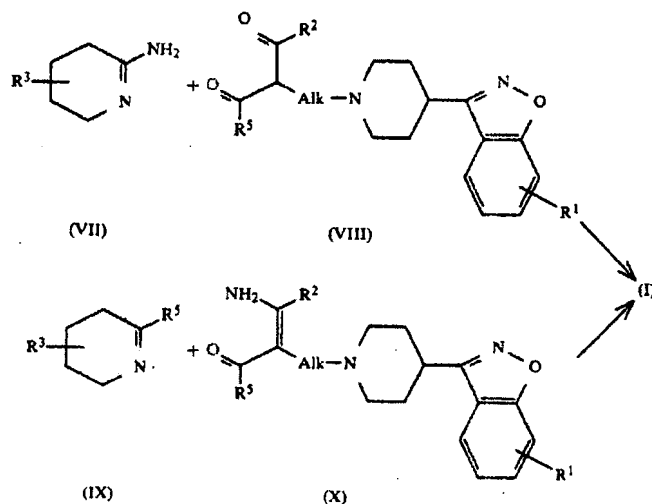
Said O-acylation reactions can conveniently be carried out by stirring the reactants optionally in a suitable reaction-inert solvent such as, for example, a halogenated hydrocarbon, e.g. dichloromethane, trichloromethane and the like; an aromatic hydrocarbon, e.g. benzene, methylbenzene and the like; an ether, e.g. 1,1'-oxybisethane, tetrahydrofuran and the like; or a dipolar aprotic solvent, e.g. N,N-dimethylformamide, N,N-dimethylacetamide, or pyridine and the like. In some instances it may be appropriate to employ an excess of one of the reagents as solvent. The water, acid, alcohol or amine which is liberated during the course of the reaction may be removed from the reaction mixture by art-known procedures such as, for example, azeotropic distillation, complexation, salt formation and the like methods. In some instances particularly the addition of a suitable base such as, for example, a tertiary amine, e.g. N,N-diethyl-ethanamine, 4-ethylmorpholine, pyridine or N,N-dimethyl-4-aminopyridine, may be appropriate. Further, in order to enhance the rate of the reaction, said acylation reaction may advantageously be conducted at a somewhat elevated temperature, and in particular instances at the reflux temperature of the reaction mixture.

The compounds of formula (I) can also be prepared following art-known cyclization procedures for preparing pyrimidin-4-ones such as, for example, by reacting an amidine of formula (VII) with a β -dicarbonyl intermediate of formula (VIII), or by cyclizing a reagent of



Alternatively, the compound of formula (I-a) and the carboxylic acid of formula (VI) may also be esterified in the presence of a suitable reagent capable of forming esters such as, for example, a dehydrating reagent, e.g. dicyclohexylcarbodiimide, 2-chloro-1-methyl-

formula (IX) with an enamine of formula (X). In formulae (VIII), (IX) and (X) R^5 represents an appropriate leaving group such as, for example, C_1 -alkyloxy, hydroxy, halo, amino, mono- or di- $(C_1$ -alkyl)amino and the like.



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Said cyclization reactions may generally be carried out by stirring the reactants, optionally in the presence of a suitable reaction-inert solvent such as, for example, an aliphatic, alicyclic or aromatic hydrocarbon, e.g. hexane, cyclohexane, benzene and the like; pyridine, N,N-dimethylformamide and the like dipolar aprotic solvents. In order to enhance the rate of the reaction it may be appropriate to increase the temperature, more particularly, it may be recommendable to carry out the reaction at the reflux temperature of the reaction mixture.

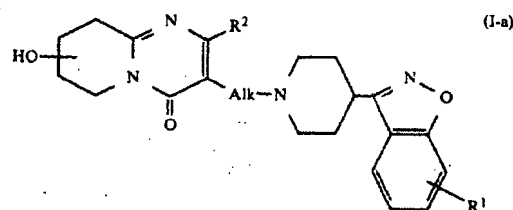
The compounds of formula (I) have basic properties and, consequently, they may be converted to their therapeutically active non-toxic acid addition salt forms by treatment with appropriate acids, such as, for example, inorganic acids, such as hydrohalic acid, e.g. hydrochloric, hydrobromic acid and the like, sulfuric acid, nitric acid, phosphoric acid and the like; or organic acids, such as, for example, acetic, propanoic, hydroxyacetic, 2-hydroxypropanoic, 2-oxopropanoic, ethanedioic, propanedioic, butanedioic, (Z)-2-butenedioic, (E)-2-butenedioic, 2-hydroxybutanedioic, 2,3-dihydroxybutanedioic, 2-hydroxy-1,2,3-propanetricarboxylic, methanesulfonic, ethanesulfonic, benzenesulfonic, 4-methylbenzenesulfonic, cyclohexanesulfamic, 2-hydroxybenzoic, 4-amino-2-hydroxybenzoic and the like acids. Conversely the salt form can be converted into the free base form by treatment with alkali.

The term acid addition salt as used hereinabove also comprises the solvates which the compounds of formula (I) are able to form and said solvates are meant to be included within the scope of the present invention. Examples of such solvates are e.g., the hydrates, alcoh-

olates and the like.

Enantiomeric forms of the compounds of formula (I-a)

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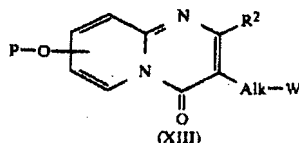
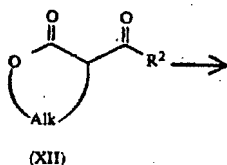
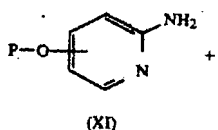


can be obtained by converting the racemic mixtures of the compounds of formula (I-a) with a suitable resolving reagent such as, for example, a chiral acid, e.g. tartaric, malic and mandelic acids, campher sulfonic acid, 4,5-dihydro-1H-2-benzopyran-2-carboxylic acid and the like, or the reactive functional derivatives thereof, e.g. the acyl halides, to a mixture of diastereomeric salts or compounds, particularly esters; physically separating said mixtures of diastereomeric salts or compounds by, for example, selective crystallization or chromatographic techniques, e.g. liquid chromatography and the like methods; and finally converting said separated diastereomeric salts or compounds into the corresponding enantiomeric forms of the compounds of formula (I-a) by hydrolysis in an acidic or basic aqueous medium, optionally at an elevated temperature.

Some of the intermediates and starting materials for use in the foregoing preparations are known compounds, while others are novel. The intermediates of formula (II) and methods of preparing them are known from EP-A-0,196,132. The alkylating reagents of formula (III) are novel and can be prepared according to art-known methodologies of preparing similar compounds and will be described hereinafter in more detail.

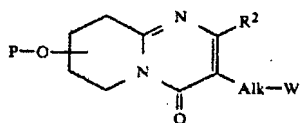
By condensing an optionally protected 2-aminopyridine derivative (XI) with an α -acyl lactone (XII) in the presence of an activating reagent in a suitable reaction-inert solvent, an intermediate of formula (XIII) can be obtained.

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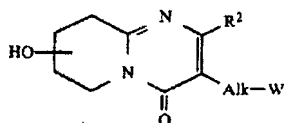


In the formulae (XI), (XIII) and hereinafter whenever it occurs, P represents hydrogen or a protective group which can be readily removed such as, for example, a hydrogenolyzable group, e.g. phenylmethyl and the like; a hydrolyzable group, e.g. methyl and the like. Appropriate activating reagents for said condensation reaction typically are halogenating reagents such as, for example, phosphoryl chloride, phosphoryl bromide, phosphorous trichloride, thionyl chloride and the like reagents.

The subsequent catalytic hydrogenation of intermediate (XIII) in a suitable reaction-inert solvent in the presence of hydrogen, optionally at an elevated temperature and/or pressure, with a catalyst such as, for example, palladium-on-charcoal and the like, can yield a protected intermediate (XIV) in case P is an alkyl group such as, for example, methyl;



or, on the other hand, when P is hydrogen or a hydrogenolyzable group such as, for example, phenylmethyl, an alkylating reagent of formula (III-a) wherein R^3 is hydroxy can be obtained directly.

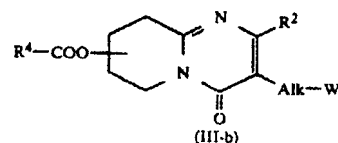


Suitable solvents for said catalytic hydrogenation reaction comprise water; C_{1-4} alkanols, e.g. methanol, ethanol, 2-propanol and the like; ethers, e.g. 1,1'-oxybis-

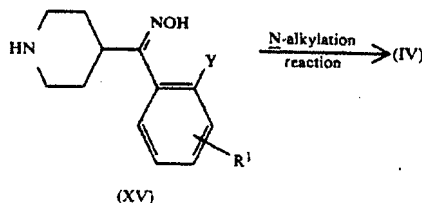
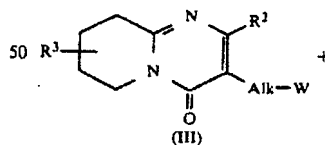
thane, 1,4-dioxane, tetrahydrofuran, 2-methoxyethanol and the like; halogenated hydrocarbons, e.g. trichloromethane and the like; dipolar aprotic solvents, e.g. N,N-dimethylformamide and the like; esters, e.g. ethyl acetate, butyl acetate and the like; or a mixture of such solvents.

The intermediate (XIV) wherein P represents an alkyl group may be deprotected to a reagent of formula (III-a) by heating the former with concentrated hydrobromic or hydroiodic acid or by reaction with Lewis acids such as, for example, boron trihalides, e.g. boron trifluoride, boron trichloride and in particular boron tribromide; iodotrimethylsilane; or aluminum chloride and the like Lewis acids.

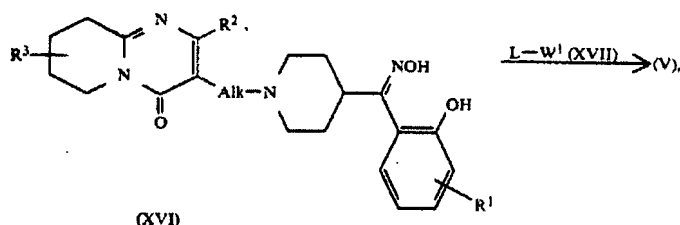
The intermediate of formula (III-a) may be O-acylated with a carboxylic acid of formula (VI) or a functional derivative thereof as defined hereinabove, to an alkylating reagent of formula (III-b) wherein R^3 is $R^4-C(=O)-O-$ following the same procedures as described hereinabove for the O-acylation of the compounds of formula (I-a).



The intermediates of formula (IV) may be prepared by N-alkylating a reagent of formula (III) with an oxime derivative of formula (XV) following the same procedures as described hereinabove for the preparation of the compounds of formula (I) from the intermediates (II) and (III). The derivatives (XV) are known from EP-A-0,196,132.

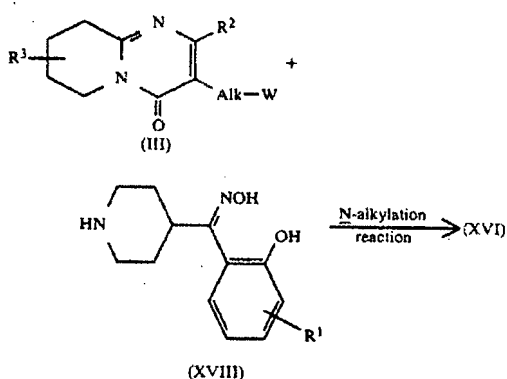


The intermediates of formula (V) may be obtained by reacting an oxime of formula (XVI) with an activated acid derivative of formula L-W¹ (XVII),



wherein L is an acid residue as defined hereinabove and W¹ represents a reactive leaving group such as, for example, halo, (aryl or C₁-alkyl)carbonyloxy, (aryl or C₁-alkyl)oxy and the like. As typical examples of the reagent of formula (XVII) there may be mentioned carboxylic acid anhydrides, e.g. acetic anhydride, benzoic anhydride and the like; carboxylic acid halides, e.g. acetyl chloride, benzoyl chloride and the like; carbonochlorides, e.g. methyl, ethyl or phenyl carbonochloride and the like; di(C₁-alkyl)carbonates, e.g. dimethylcarbonate, diethylcarbonate and the like. The reaction of the intermediates (XVI) with the activated acid derivatives (XVII) may be carried out following art-known esterification procedures, e.g. by stirring the reactants at a somewhat elevated temperature, preferably in a reaction-inert solvent such as, for example, an aromatic hydrocarbon, e.g. benzene, methylbenzene and the like; a halogenated hydrocarbon, e.g. dichloromethane, trichloromethane and the like; a ketone, e.g. 2-propanone, 4-methyl-2-pentanone and the like; an ether, e.g. 1,1'-oxybisethane, 1,4-dioxane and the like; a dipolar aprotic solvent, e.g. N,N-dimethylformamide, pyridine and the like solvents. In some instances it may be appropriate to add a suitable base such as, for example, N,N-diethylethanamine, N-(1-methylethyl)-2-propanamine, 4-ethylmorpholine, N,N-dimethyl-4-aminopyridine and the like bases to the reaction mixture.

The intermediate of formula (XVI) in turn may be prepared by N-alkylating a reagent of formula (III) with an oxime derivative of formula (XVIII)



following the same procedures as described hereinabove for the preparation of the compounds of formula (I) from the intermediates (II) and (III).

The compounds of formula (I) and some of the intermediates in the present invention contain at least one asymmetric carbon atom. Pure stereochemically isomeric forms of said compounds and said intermediates

can be obtained by the application of art-known procedures. For example, diastereoisomers can be separated by physical methods such as selective crystallization or chromatographic techniques, e.g. counter current distribution, liquid chromatography and the like methods. Enantiomers can be obtained from racemic mixtures by first converting said racemic mixtures with suitable resolving agents such as, for example, chiral acids, to mixtures of diastereomeric salts or compounds; then physically separating said mixtures of diastereomeric salts or compounds by, for example, selective crystallization or chromatographic techniques, e.g. liquid chromatography and the like methods; and finally converting said separated diastereomeric salts or compounds into the corresponding enantiomers.

Pure stereochemically isomeric forms of the compounds of formula (I) may also be obtained from the pure stereochemically forms of the appropriate intermediates and starting materials, provided that the intervening reactions occur stereospecifically. The pure and mixed stereochemically isomeric forms of the compounds of formula (I) are intended to be embraced within the scope of the present invention.

The compounds of formula (I), the pharmaceutically acceptable acid addition salts and stereochemically isomeric forms thereof, are potent antagonists of neurotransmitters and in particular of the mediators serotonin and dopamine. Antagonizing said mediators will suppress or relieve a variety of symptoms associated with phenomena induced by the release, in particular the excessive release, of these mediators. Therapeutic indications for using the present compounds are mainly in the CNS area, the gastrointestinal and cardiovascular field and related domains. The compounds of formula (I) are particularly useful as antipsychotic agents. Serotonin antagonists are reportedly effective in combatting psychoses, aggressive behaviour, anxiety, depression and migraine. Dopamine receptor antagonists are known to have neuroleptic properties. Combined serotonin-dopamine antagonists are especially interesting as they appear to offer relief of both the positive and negative symptoms of schizophrenia. Further the present compounds also appear to be useful therapeutic agents for combatting autism. Therapeutic applications in the gastrointestinal field comprise their use as, for instance, anti-diarrhoeals, inhibitors of gastro-oesophageal reflux and particularly antiemetics, e.g. in cancer patients receiving chemotherapy and radiation treatment. Further, serotonin is a potent broncho- and vasoconstrictor and thus the present antagonists may be used against hypertension and vascular disorders. In addition, serotonin antagonists have been associated with a number of other properties such as, the suppression of appetite and promotion of weight loss, which may prove effective in combating obesity; and also the

alleviation of withdrawal symptoms in addicts trying to discontinue drinking and smoking habits.

The compounds of formula (I) show the additional advantage of being eliminated rather slowly from the body and thus of being long acting. This can be evidenced, for example, by measuring the plasma levels after oral administration to dogs and by the long acting antiemetic effect exerted by the present compounds on dogs challenged with the dopamine agonist apomorphine. Especially the compounds of formula (I) wherein R^3 is a higher alkylcarbonyloxy radical have a long duration of action. Hence, the compounds of formula (I) only need to be administered at relatively large intervals, e.g. several days or weeks, the actual time of administration depending on the nature of the compound of formula (I) used and the condition of the subject to be treated. Consequently, the present compounds allow for a more efficient therapy: the slow elimination facilitates maintaining a stable plasma concentration at a non-toxic, effective level and the reduction in the number of administrations may be expected to result in better compliance of the subject to be treated with the prescribed medication.

In view of their useful pharmacological properties, the subject compounds may be formulated into various pharmaceutical forms for administration purposes. To prepare the pharmaceutical compositions of this invention, an effective amount of the particular compound, in acid addition salt or base form, as the active ingredient is combined in intimate admixture with a pharmaceutically acceptable carrier, which may take a wide variety of forms depending on the form of preparation desired for administration. These pharmaceutical compositions are desirably in unitary dosage form suitable, preferably, for administration orally, rectally, percutaneously, or by parenteral injection. For example, in preparing the compositions in oral dosage form, any of the usual pharmaceutical media may be employed, such as, for example, water, glycols, oils, alcohols and the like in the case of oral liquid preparations such as suspensions, syrups, elixirs and solutions; or solid carriers such as starches, sugars, kaolin, lubricants, binders, disintegrating agents and the like in the case of powders, pills, capsules and tablets. Because of their ease in administration, tablets and capsules represent the most advantageous oral dosage unit form, in which case solid pharmaceutical carriers are obviously employed. For parenteral compositions, the carrier will usually comprise sterile water, at least in large part, though other ingredients, for example, to aid solubility, may be included. Injectable solutions, for example, may be prepared in which the carrier comprises saline solution, glucose solution or a mixture of saline and glucose solution. Injectable solutions containing compounds of formula (I) wherein R^3 is $R^4-C(=O)-O-$ may be formulated in an oil for prolonged action. Appropriate oils for this purpose are, for example, peanut oil, sesame oil, cottonseed oil, corn oil, soy bean oil, synthetic glycerol esters of long chain fatty acids and mixtures of these and other oils. Injectable suspensions may also be prepared in which case appropriate liquid carriers, suspending agents and the like may be employed. In the compositions suitable for percutaneous administration, the carrier optionally comprises a penetration enhancing agent and/or a suitable wettable agent, optionally combined with suitable additives of any nature in minor proportions, which additives do not cause any significant deleterious effects on the skin. Said additives may facilitate

the administration to the skin and/or may be helpful for preparing the desired compositions. These compositions may be administered in various ways, e.g., as a transdermal patch, as a spot-on or as an ointment. Acid addition salts of (I) due to their increased water solubility over the corresponding base form, are obviously more suitable in the preparation of aqueous compositions.

It is especially advantageous to formulate the aforementioned pharmaceutical compositions in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used in the specification and claims herein refers to physically discrete units suitable as unitary dosages, each unit containing a predetermined quantity of active ingredient calculated to produce the desired therapeutic effect, in association with the required pharmaceutical carrier. Examples of such dosage of unit forms are tablets (including scored or coated tablets), capsules, pills, powder packets, wafers, injectable solutions or suspensions, teaspoonfuls, tablespoonfuls and the like, and segregated multiples thereof.

In view of the usefulness of the subject compounds in the treatment of diseases associated with the release of neurotransmitters, in particular in the treatment of psychotic diseases, it is evident that the present invention provides a method of treating warm-blooded animals suffering from such diseases, in particular psychotic diseases, said method comprising the systemic administration of an antipsychotic amount of a compound of formula (I) or a pharmaceutically acceptable acid addition salt thereof, effective in treating diseases associated with the release of neurotransmitters, in particular psychotic diseases. Those of skill in the treatment of such diseases could easily determine the effective amount from the test results presented hereinafter. In general it is contemplated that an effective antipsychotic amount would be from about 0.01 mg/kg to about 4 mg/kg body weight, more preferably from about 0.04 mg/kg to about 2 mg/kg body weight.

The following examples are intended to illustrate and not to limit the scope of the present invention. Unless otherwise stated all parts therein are by weight.

EXPERIMENTAL PART

A. Preparation of Intermediates

EXAMPLE 1

a) To a stirred mixture of 84 parts of phosphoryl chloride and 540 parts of methylbenzene were added 20 parts of 3-(phenylmethoxy)-2-pyridinamine. The mixture was stirred at 50° C. and 22 parts of 3-acetyl-4,5-dihydro-2(3H)-furanone were added. The reaction mixture was stirred for 5 hours at 90° C. Another portion of 22 parts of 3-acetyl-4,5-dihydro-2(3H)-furanone was added and stirring was continued for 30 minutes at 90° C. The solution was allowed to stand overnight at 90° C. The whole was poured into crushed ice and treated with an ammonium hydroxide solution 25%. The product was extracted with trichloromethane. The extract was dried, filtered and evaporated. The residue was purified by column chromatography over silica gel using a mixture of trichloromethane and methanol (98:2 by volume) as eluent. The pure fractions were collected and the eluent was evaporated. The residue was stirred in 2-propanol. The product was filtered off, washed with a mixture of 2-propanol and 1,1'-oxybisethane and dried at 50° C., yielding 20.5 parts (62.3%) of 3-(2-chloroethyl)-2-methyl-9-(phenylmethoxy)-4H-

pyrido[1,2-a]pyrimidin-4-one; mp. 141.1° C. (intermediate 1)

b) A mixture of 3.3 parts of 3-(2-chloroethyl)-2-methyl-9-(phenylmethoxy)-4H-pyrido[1,2-a]pyrimidin-4-one and 120 parts of methanol was hydrogenated at normal pressure and at room temperature with 2.0 parts of palladium-on-charcoal catalyst 10%. After the calculated amount of hydrogen was taken up, the catalyst was filtered off and the filtrate was evaporated to dry, yielding 2.4 parts (99%) of 3-(2-chloroethyl)-6,7,8,9-tetrahydro-9-hydroxy-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one as an oily residue. (intermediate 2)

EXAMPLE 2

a) A mixture of 17 parts of 5-methoxy-2-pyridinamine, 61 parts of phosphoryl chloride and 348 parts of methylbenzene was stirred for 2 hours at 60° C. 18 Parts of 3-acetyl-4,5-dihydro-2(3H)-furanone were added and the reaction mixture was stirred overnight at 90° C. The whole was poured into crushed ice and treated with ammonium hydroxide. The product was extracted with trichloromethane. The extract was dried, filtered and evaporated. The residue was stirred in a mixture of hexane and ethyl acetate (50:50 by volume). The precipitated product was filtered off and dried, yielding 10 parts (30.4%) of 3-(2-chloroethyl)-7-methoxy-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one; mp. 150° C. (intermediate 3)

b) A mixture of 10 parts of 3-(2-chloroethyl)-7-methoxy-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one, 40 parts of 2-propanol saturated with hydrogen chloride and 160 parts of methanol was hydrogenated at normal pressure and at room temperature with 2.0 parts of palladium-on-charcoal catalyst 10%. After the calculated amount of hydrogen was taken up, the catalyst was filtered off over diatomaceous earth and the filtrate was evaporated. The oily residue was taken up in 80 parts of 2-propanol and 2,2'-oxybispropane. After stirring overnight at room temperature, the precipitated product was filtered off, washed with a mixture of 2-propanol and 2,2'-oxybispropane and dried in vacuo at 50° C., yielding 7.5 parts (64.0%) of 3-(2-chloroethyl)-6,7,8,9-tetrahydro-7-methoxy-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one monohydrochloride; mp. 170° C. (intermediate 4)

c) A mixture of 6 parts of 3-(2-chloroethyl)-6,7,8,9-tetrahydro-7-methoxy-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one, 4.8 parts of 6-fluoro-3-(4-piperidinyl)-1,2-benzisoxazole monohydrochloride, 6.1 parts of N-(1-methylethyl)-2-propanamine and 16 parts of methanol was stirred overnight at reflux temperature. The reaction mixture was evaporated and the residue was taken up in water. The product was extracted with trichloromethane. The extract was dried, filtered and evaporated. The residue was purified by column chromatography over silica gel using a mixture of trichloromethane and methanol (95:5 by volume) as eluent. The pure fractions were collected and the eluent was evaporated, yielding 8.5 parts (100%) of 3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-7-methoxy-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one as an oily residue. (intermediate 5)

B. Final Compounds

EXAMPLE 3

A mixture of 12.5 parts of 3-(2-chloroethyl)-6,7,8,9-tetrahydro-9-hydroxy-4H-pyrido[1,2-a]pyrimidin-4-one, 10.0 parts of 6-fluoro-3-(4-piperidinyl)-1,2-ben-

zisoxazole monohydrochloride, 10 parts of N-(1-methylethyl)-2-propanamine and 120 parts of methanol was stirred overnight at 60° C. The reaction mixture was evaporated and the oily residue was taken up in trichloromethane and washed with water. The organic layer was dried, filtered and evaporated. The residue was purified twice by column chromatography over silica gel first using a mixture of trichloromethane and methanol (95:5 by volume) and then a mixture of trichloromethane and methanol, saturated with ammonia (95:5 by volume) as eluents. The pure fractions were collected and the eluent was evaporated. The residue was crystallized from 2-propanone. After cooling, the precipitated product was filtered off, washed with a mixture of 2-propanol and 2,2'-oxybispropane and recrystallized from 2-propanol. The product was filtered off and dried, yielding 3.6 parts (21.1%) of 3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-9-hydroxy-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one; mp. 179.8° C. (Compound 1)

EXAMPLE 4

To a stirred solution of 5.4 parts of 3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-9-hydroxy-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one and 1.6 parts of N,N-dimethyl-4-pyridinamine in 39 parts of dichloromethane was added dropwise a solution of 5.4 parts of (+)-3,4-dihydro-1H-2-benzopyran-2-carbonyl chloride in 39 parts of dichloromethane. Upon complete addition, stirring was continued for 4 hours at room temperature. The reaction mixture was washed successively with water, a sodium hydroxide solution 1N and water, dried, filtered and evaporated. The residue was purified by column chromatography over silica gel using a mixture of acetonitrile and water, saturated with ammonia (50:50 by volume) as eluent. Two pure fractions were collected and the eluent was evaporated. Each residue was salted out with sodium chloride and two diastereo-isomeric esters were obtained. The first isomer was combined with 16 parts of methanol, 1 part of N-(1-methylethyl)-2-propanamine and 1 part of water and the whole was stirred for 160 minutes at 60° C. The mixture was evaporated and the residue was purified by column chromatography over silica gel using a mixture of trichloromethane and methanol (90:10 by volume) as eluent. The pure fractions were collected and the eluent was evaporated. The residue was crystallized from 2-propanol. The product was filtered off and dried, yielding 0.2 parts (3.6%) of (+)-3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-9-hydroxy-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one; mp. 160.7° C., $[\alpha]_D^{25} = +15.42^\circ$ (c=0.5% in ethanol). (Compound 2)

The second isomer was combined with 16 parts of methanol, 1 part of N-(1-methylethyl)-2-propanamine and 1 part of water and the whole was stirred for 160 minutes at 60° C. The mixture was evaporated and the residue was purified by column chromatography over silica gel using a mixture of trichloromethane and methanol (90:10 by volume) as eluent. The pure fractions were collected and the eluent was evaporated. The residue was crystallized from 2-propanol. The product was filtered off and dried, yielding 0.2 parts (3.6%) of (-)-3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-9-hydroxy-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one; mp. 156.9° C., $[\alpha]_D^{25} = -22.81^\circ$ C. (c=0.5% in ethanol). (Compound 3)

EXAMPLE 5

A mixture of 4.3 parts of 3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-9-hydroxy-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one and 30 parts of acetic acid anhydride was stirred for 4 hours at 50° C. After cooling, the reaction mixture was poured into water and treated with an ammonium hydroxide solution. The product was extracted with 4-methyl-2-pentanone. The extract was dried, filtered and evaporated. The residue was purified by column chromatography over silica gel using a mixture of trichloromethane and methanol (95:5 by volume) as eluent. The pure fractions were collected and the eluent was evaporated in vacuo. The residue was crystallized from 2,2'-oxybispropane. The product was filtered off and dried, yielding 3.0 parts (64.0%) of 3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-2-methyl-4-oxo-4H-pyrido[1,2-a]pyrimidin-9-acetate (ester); mp. 143.6° C. (Compound 4) In a similar manner and by using butanoic acid anhydride as acylating reagent there was also prepared [3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-2-methyl-4-oxo-4H-pyrido[1,2-a]pyrimidin-9-yl]butanoate, mp. 112.9° C. (Compound 5).

EXAMPLE 6

To a stirred solution of 1.2 parts of 3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-9-hydroxy-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one in 21 parts of dichloromethane and 5 parts of water were simultaneously added dropwise a solution of 1.1 parts of decanoyl chloride in 13 parts of dichloromethane and a solution of 1 part of sodium hydroxide in 6 parts of water. Upon complete addition, stirring was continued for 2 hours at room temperature. Another portion of 1.1 parts of decanoyl chloride was added and stirring was continued overnight at room temperature. The product was extracted with dichloromethane. The extract was washed with water, dried, filtered and evaporated. The residue was purified by column chromatography over silica gel using a mixture of trichloromethane and methanol (95:5 by volume) as eluent. The pure fractions were collected and the eluent was evaporated. The residue was converted into the hydrochloride salt in 2-propanol. The product was filtered off and dried, yielding 0.9 parts (45.9%) of [3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-2-methyl-4-oxo-4H-pyrido[1,2-a]pyrimidin-9-yl]decanoate dihydrochloride; mp. 221.4° C. (Compound 6)

EXAMPLE 7

A mixture of 8.5 parts of 3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-7-methoxy-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one, 14 parts of iodotrimethylsilane and 40 parts of acetone was stirred overnight at 70° C. Another portion of 2.8 parts of iodotrimethylsilane was added and the reaction mixture was stirred for a while at 90° C. and then overnight at reflux temperature. After cooling, the whole was evaporated. The residue was taken up in ethanol and the whole was evaporated again. The residue was taken up in water and treated with a sodium hydroxide solution. The product was extracted with trichloromethane. The extract was dried, filtered and evaporated. The residue was purified by column chromatography over silica gel using a mixture of trichloro-

methane and methanol (95:5 by volume) as eluent. The desired fraction was collected and the eluent was evaporated. The residue was solidified in ethanol. The product was filtered off and dried, yielding 0.3 parts (3.7%) of 3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-7-hydroxy-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one; mp. 156.2° C. (Compound 7)

Following the procedure of example 6, compound 7 was converted to [3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-2-methyl-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-yl]decanoate. (Compound 8)

C. Pharmacological Examples

EXAMPLE 8

The antipsychotic activity of the subject compounds is evidenced by the experimental data obtained in at least one of two different test procedures, viz. the combined apomorphine (APO), tryptamine (TRY) and norepinephrine (NOR) test in rats, and the apomorphine test in dogs. Said combined apomorphine, tryptamine and norepinephrine test is described in Ach. int. Pharmacodyn., 227, 238-253 (1977) and provides an empirical evaluation of the relative specificity with which drugs may effect particular neurotransmitter systems centrally (CNS) as well as peripherally. In particular, the test demonstrates the antagonistic activity of the tested compounds of formula (I) on dopamine (by preventing the symptoms elicited with the dopamine agonist apomorphine), on serotonin (by preventing the central and peripheral symptoms (convulsions; hyperemia) elicited with serotonin or tryptamine), and on norepinephrine (by preventing or delaying death upon administration of the α_2 -agonist norepinephrine). Said apomorphine test in dogs is described in Arzneim.-Forsch. (Drug Res.), 9, 765-767 (1959) and provides a measure of the duration of action of the tested compounds. The tests are carried out following the procedures described in EP-A-0,196,132 and the experimental data are summarized in Table 1.

TABLE I

Comp No.	Combined test in rats; ED ₅₀ in mg/kg				(APO)-dog test, ED ₅₀ in mg/kg		
	(APO)	(TRY)-convulsions	(TRY)-hyperemia	(NOR)	1 hr	4 hr	16 hr
1	0.25	0.31	0.002	0.08	0.015	0.015	0.015
2	0.31	0.08	0.00031	1.25	0.015	0.03	0.06
3	0.31	0.31	0.00063	0.63	0.008	0.007	0.015
4	0.31	0.08	0.00031	0.31	0.015	*	*
5	0.31	0.31	0.00125	0.16	0.008	*	*

*not tested.

D. Composition Examples

EXAMPLE 9

Oral Drops

500 Parts of the A.I. was dissolved in 0.5 l of 2-hydroxypropanoic acid and 1.5 l of the polyethylene glycol at 60°-80° C. After cooling to 30°-40° C. there were added 35 l of polyethylene glycol and the mixture was stirred well. Then there was added a solution of 1750 parts of sodium saccharin in 2.5 l of purified water and while stirring there were added 2.5 l of cocoa flavor and polyethylene glycol q.s. to a volume of 50 l, providing an oral drop solution comprising 10 mg/ml of A.I..

The resulting solution was filled into suitable containers.

EXAMPLE 10

Oral Solution

9 Parts of methyl 4-hydroxybenzoate and 1 part of propyl 4-hydroxybenzoate were dissolved in 4 l of boiling purified water. In 3 l of this solution were dissolved first 10 parts of 2,3-dihydroxybutanedioic acid and thereafter 20 parts of the A.I. The latter solution was combined with the remaining part of the former solution and 12 l 1,2,3-propanetriol and 3 l of sorbitol 70% solution were added thereto. 40 Parts of sodium saccharin were dissolved in 0.5 l of water and 2 ml of raspberry and 2 ml of gooseberry essence were added. The latter solution was combined with the former, water was added q.s. to a volume of 20 l providing an oral solution comprising 5 mg of the active ingredient per teaspoonful (5 ml). The resulting solution was filled in suitable containers.

EXAMPLE 11

Capsules

20 Parts of the A.I., 6 parts sodium lauryl sulfate, 56 parts starch, 56 parts lactose, 0.8 parts colloidal silicon dioxide, and 1.2 parts magnesium stearate were vigorously stirred together. The resulting mixture was subsequently filled into 1000 suitable hardened gelatin capsules, comprising each 20 mg of the active ingredient.

EXAMPLE 12

Film-Coated Tablets

Preparation of tablet core

A mixture of 100 parts of the A.I., 570 parts lactose and 200 parts starch was mixed well and thereafter humidified with a solution of 5 parts sodium dodecyl sulfate and 10 parts polyvinylpyrrolidone (Kollidon-K 90 ®) in about 200 ml of water. The wet powder mixture was sieved, dried and sieved again. Then there was added 100 parts microcrystalline cellulose (Avicel ®) and 15 parts hydrogenated vegetable oil (Sterotex ®). The whole was mixed well and compressed into tablets, giving 10,000 tablets, each containing 10 mg of the active ingredient.

Coating

To a solution of 10 parts methyl cellulose (Methocel 60 HG ®) in 75 ml of denaturated ethanol there was added a solution of 5 parts of ethyl cellulose (Ethocel 22 cps ®) in 150 ml of dichloromethane. Then there were added 75 ml of dichloromethane and 2.5 ml 1,2,3-propanetriol. 10 Parts of polyethylene glycol was molten and dissolved in 75 ml of dichloromethane. The latter solution was added to the former and then there were added 2.5 parts of magnesium octadecanoate, 5 parts of polyvinylpyrrolidone and 30 ml of concentrated colour suspension (Opaspray K-1-2109 ®) and the whole was homogenated. The tablet cores were

coated with the thus obtained mixture in a coating apparatus.

EXAMPLE 13

Injectable Solution

1.8 Parts methyl 4-hydroxybenzoate and 0.2 parts propyl 4-hydroxybenzoate were dissolved in about 0.5 l of boiling water for injection. After cooling to about 50° C. there were added while stirring 4 parts lactic acid, 0.05 parts propylene glycol and 4 parts of the A.I.. The solution was cooled to room temperature and supplemented with water for injection q.s. ad 1 l, giving a solution comprising 4 mg/ml of A.I.. The solution was sterilized by filtration (U.S.P. XVII p. 811) and filled in sterile containers.

EXAMPLE 14

Suppositories

3 Parts A.I. was dissolved in a solution of 3 parts 2,3-dihydroxybutanedioic acid in 25 ml polyethylene glycol 400. 12 Parts surfactant (SPAN ®) and triglycerides (Witepsol 555 ®) q.s. ad 300 parts were molten together. The latter mixture was mixed well with the former solution. The thus obtained mixture was poured into moulds at a temperature of 37°-38° C. to form 100 suppositories each containing 30 mg/ml of the A.I.

EXAMPLE 15

Injectable Solution

60 Parts of A.I. and 12 parts of benzylalcohol were mixed well and sesame oil was added q.s. ad 1 l, giving a solution comprising 60 mg/ml of A.I. The solution was sterilized and filled in sterile containers.

We claim:

1. A compound selected from the group consisting of a C₂₋₂₀alkanoic acid ester of 3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-9-hydroxy-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one, a pharmaceutically acceptable acid addition salt thereof, and an enantiomeric form thereof.

2. An antipsychotic composition comprising an inert carrier and as active ingredient an antipsychotic effective amount of the compound of claim 1.

3. A method of treating warm-blooded animals suffering from psychotic diseases, which method comprises the administration to said warm-blooded animals of an antipsychotic effective amount of the compound of claim 1.

4. The compound of claim 1 wherein the alkanic acid is octanoic acid, decanoic acid, dodecanoic acid, or tetradecanoic acid.

5. The composition of claim 2 wherein the alkanic acid is octanoic acid, decanoic acid, dodecanoic acid, or tetradecanoic acid.

6. The method of claim 3 wherein the alkanic acid is octanoic acid, decanoic acid, dodecanoic acid, or tetradecanoic acid.

* * * * *

Exhibit 3

**Copy of U.S. Patent & Trademark
Office Maintenance Fee Statement
for U.S. Patent No. 5,254,556**



United States
Patent and
Trademark Office

Patent Bibliographic Data				08/24/2009 12:37 PM	
Patent Number:	5254556		Application Number:	07932142	
Issue Date:	10/19/1993		Filing Date:	08/19/1992	
Title:	NOVEL 3-PIPERIDINYL-1,2-BENZISOXAZOLES				
Status:	4th, 8th and 12th year fees paid			Entity:	Large
Window Opens:	N/A	Surcharge Date:	N/A	Expiration:	N/A
Fee Amt Due:	Window not open	Surchg Amt Due:	Window not open	Total Amt Due:	Window not open
Fee Code:					
Surcharge Fee Code:					
Most recent events (up to 7):	03/29/2005 Payment of Maintenance Fee, 12th Year, Large Entity. 03/16/2001 Payment of Maintenance Fee, 8th Year, Large Entity. 03/25/1997 Payment of Maintenance Fee, 4th Year, Large Entity. --- End of Maintenance History ---				
Address for fee purposes:	AUDLEY A. CIAMPORCERO JOHNSON AND JOHNSON ONE JOHNSON AND JOHNSON PLAZA NEW BRUNSWICK, NJ 089337003				
Run Another Query					



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AUDLEY A. CIAMPORCERO
JOHNSON AND JOHNSON
ONE JOHNSON AND JOHNSON PLAZA
NEW BRUNSWICK NJ 08933-7003

MAINTENANCE FEE STATEMENT

According to the records of the U.S. Patent and Trademark Office (USPTO), the maintenance fee and any necessary surcharge have been timely paid for the patent listed below. The "PYMT DATE" column indicates the payment date (i.e., the date the payment was filed).

The payment shown below is subject to actual collection. If the payment is refused or charged back by a financial institution, the payment will be void and the maintenance fee and any necessary surcharge unpaid.

Direct any questions about this statement to: Mail Stop M Correspondence, Director of the USPTO, P.O.Box 1450, Alexandria, VA 22313-1450.

PATENT NUMBER	FEE AMT	SUR CHARGE	PYMT DATE	U.S. APPLICATION NUMBER	PATENT ISSUE DATE	APPL. FILING DATE	PAYMENT YEAR	SMALL ENTITY?	ATTY DKT NUMBER
5,254,556	\$1,020.00	\$0.00	03/25/97	07/932,142	10/19/93	08/19/92	04	NO	JAB-828



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Direct any questions about this statement to: Mail Stop M Correspondence, Director of the USPTO, P.O. Box 1450, Alexandria, VA 22313-1450.

PATENT NUMBER	FEE AMT	SUR CHARGE	PYMT DATE	U.S. APPLICATION NUMBER	PATENT ISSUE DATE	APPL. FILING DATE	PAYMENT YEAR	SMALL ENTITY?	ATTY DKT NUMBER
5,254,556	\$1,950.00	\$0.00	03/16/01	07/932,142	10/19/93	08/19/92	08	NO	JAB-828



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MAINTENANCE FEE STATEMENT

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The payment shown below is subject to actual collection. If the payment is refused or charged back by a financial institution, the payment will be void and the maintenance fee and any necessary surcharge unpaid.

Direct any questions about this statement to: Mail Stop M Correspondence, Director of the USPTO, P.O. Box 1450, Alexandria, VA 22313-1450.

PATENT NUMBER	FEE AMT	SUR CHARGE	PYMT DATE	U.S. APPLICATION NUMBER	PATENT ISSUE DATE	APPL. FILING DATE	PAYMENT YEAR	SMALL ENTITY?	ATTY DKT NUMBER
5,254,556	\$3,800.00	\$0.00	03/29/05	07/932,142	10/19/93	08/19/92	12	NO	JAB-828

Exhibit 4

**Terminal Disclaimer filed in
U.S. Patent No. 5,254,556**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Cornelius G. M. Janssen et al.

Serial No. : 07/932,142 Art Unit: 1202

Filed : August 19, 1992 Examiner: J. Venkat

For : NOVEL 3-PIPERIDINYL-1,2-BENZISOXAZOLES

Honorable Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Sir:

TERMINAL DISCLAIMER

Your Petitioner, JANSSEN PHARMACEUTICA N.V., a corporation of Belgium, having an address at Turnhoutseweg 30, B-2340 Beerse, Belgium, represents that it is the Assignee of the entire right, title and interest in and to the subject matter disclosed in the above-captioned patent application by virtue of its being a divisional of U.S. Patent Application Serial No. 07/422,847, filed October 17, 1989, which was assigned to JANSSEN PHARMACEUTICA N.V., the assignment being recorded in the United States Patent and Trademark Office on November 13, 1989, on Reel 5171, Frame 0567.

Your Petitioner, JANSSEN PHARMACEUTICA N.V., hereby disclaims, under the provisions of 35 U.S.C. 253, the terminal part of any patent granted on application Serial No. 07/932,142 which would extend beyond the expiration date of United States Patent No. 5,158,952, also assigned to JANSSEN PHARMACEUTICA N.V. (recorded on November 13, 1989, on Reel 5171, Frame 0567), and hereby agrees that any patent so granted on application Serial No. 07/932,142 shall be enforceable only for and during such period that the legal title of said patent shall be the same as the legal title to United States Patent No. 5,158,952, this agreement to run with any patent granted on application Serial No. 07/932,142 and to be binding upon the grantee, its successors or assigns.

Signed at Beerse (Belgium) this 7th day of December, 1992.

Respectfully submitted,

JANSSEN PHARMACEUTICA N.V.

By: Wantet December 7, 1992

Dirk Wante

Head Patent Department, Proxy Holder

Charles J. Metz
Attorney for Applicants
Reg. # 20,359
Johnson & Johnson
One Johnson & Johnson Plaza
New Brunswick, NJ 08933-7003

(908) 524-2814

Exhibit 5**Claims 1, 2 and 3 of U.S. Patent No. 5,254,556
Claim the Active Ingredient of the Product
Seeking Approval or its Method of Use**

1. A compound selected from the group consisting of a C ₂₋₂₀ alkanoic acid ester of 3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]- 6,7,8,9-tetrahydro-9-hydroxy-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one, a pharmaceutically acceptable acid addition salt thereof, and an enantiomeric form thereof.	Paliperidone palmitate is a C ₁₆ alkanoic acid ester of 3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]- 6,7,8,9-tetrahydro-9-hydroxy-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one.
2. An antipsychotic composition comprising an inert carrier and as active ingredient an antipsychotic effective amount of the compound of claim 1.	The Product currently undergoing regulatory review comprises paliperidone palmitate, a C ₁₆ alkanoic acid ester of 3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]- 6,7,8,9-tetrahydro-9-hydroxy-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one, and one or more inert carriers provided in an amount sufficient to treat schizophrenia (a psychotic disorder).
3. A method of treating warm-blooded animals suffering from psychotic diseases, which method comprises the administration to said warm-blooded animals of an antipsychotic effective amount of the compound of claim 1.	The Product is currently undergoing regulatory review for the treatment of schizophrenia (a psychotic disease). The treatment comprises administering an antipsychotic effective amount of paliperidone palmitate, a C ₁₆ alkanoic acid ester of 3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]- 6,7,8,9-tetrahydro-9-hydroxy-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one.

Exhibit 6

**Description of Significant Activities of
Applicant during Regulatory Review**

Date	Submission Type	Date of Contact	Description	Protocol #	SNF	EDMS or Sequence #	Hyperlink	Gateway Receipt
5/6/2003	Original IND	na	Original IND (50 Volumes)	na	000	Multiple	Original IND	na
5/13/2007	Record of Contact	5/13/2003	Request for Additional Desk Copies and IND Number for Paliperidone palmitate	na	na	2651976	EDMS-PSDB-2651976	na
5/19/2003	Record of Contact	5/19/2003	Request for List of Nonclinical Studies Submitted Under IND 67,356	na	na	2656702	EDMS-PSDB-2656702	na
5/28/2003	General Correspondence	na	Response to Request by Review Chemist	na	001	2676686	EDMS-PSDB-2676686	na
5/30/2003	General Correspondence	na	Response to Request from Dr. Lois Freed	na	002	2683477	EDMS-PSDB-2683477	na
6/2/2003	Record of Contact	6/2/2003	Clearance to Proceed with the Studies Under IND	na	na	2697285	EDMS-PSDB-2697285	na
6/5/2003	General Correspondence	na	Response to Request by Review Chemist	na	003	2716903	EDMS-PSDB-2716903	na
9/11/2003	Protocol Amendment	na	New Investigators	R092670-USA-3	004	2931978	EDMS-PSDB-2931978	na
9/12/2003	Information Amendment	na	CMC, Pharmacology/Toxicology	na	005	2937288	EDMS-PSDB-2937288	na
10/28/2003	Protocol Amendment	na	New Protocol, New Investigator	R092670-SCH-201	006	3044512	EDMS-PSDB-3044512	na
1/9/2004	Protocol Amendment	na	New Investigators	R092670-SCH-201	007	3195694	EDMS-PSDB-3195694	na
1/23/2004	Protocol Amendment	na	New Investigators	R092670-SCH-201	008	3230681	EDMS-PSDB-3230681	na
2/11/2004	Protocol Amendment	na	New Investigators	R092670-SCH-201	009	3288697	EDMS-PSDB-3288697	na
3/31/2004	Safety Report	na	US-JNJFOC-20040304794 Initial	R076477-SCH-304	010	3397560	EDMS-PSDB-3397560	na
4/22/2004	General Correspondence	na	Request for Type B End of Phase 2 Meeting - Chemistry, Microbiology, and Biopharmaceutics	na	011	3442328	EDMS-PSDB-3442328	na
4/29/2004	FDA Correspondence	na	Letter: Meeting Request Granted for 6/16/04	na	na	3548304	EDMS-PSDB-3548304	na
5/6/2004	General Correspondence	na	Request for a Type B End-of-Phase 2 Meeting	na	012	3474299	EDMS-PSDB-3474299	na
5/10/2004	Safety Report	na	US-JNJFOC-20040304794 F-1	R076477-SCH-304	013	3479851	EDMS-PSDB-3479851	na
5/20/2004	General Correspondence	na	Briefing Package for 6/16/04 CMC/Biopharm Meeting	na	014	3514273	EDMS-PSDB-3514273	na
6/16/2004	Record of Contact	6/16/2004	Minutes of 6/16/04 CMC/Biopharmaceutics End of Phase 2 Meeting for Paliperidone palmitate	na	na	3594054	EDMS-PSDB-3594054	na
6/28/2004	General Correspondence	na	Minutes of 6/16/04 Type B End of Phase 2 Meeting - CMC/Biopharmaceutics	na	015	3599384	EDMS-PSDB-3599384	na
7/1/2004	Protocol Amendment	na	New Investigators	R092670-SCH-201	016	3609437	EDMS-PSDB-3609437	na
8/4/2004	Annual Report	na	Reporting Period: 6/7/03 - 6/6/04	na	017	3681428	EDMS-PSDB-3681428	na
8/12/2004	Safety Report	na	IN-JNJFOC-20040800656 Initial	R076477-SCH-303	018	3699361	EDMS-PSDB-3699361	na
8/17/2004	Protocol Amendment	na	New Investigators	R092670-SCH-201	019	3704542	EDMS-PSDB-3704542	na
8/25/2004	Safety Report	na	IN-JNJFOC-20040800656 F-1	R076477-SCH-303	020	3723435	EDMS-PSDB-3723435	na
8/27/2004	General Correspondence	na	Notice of Intent to Request Special Protocol Assessment: Carcinogenicity	na	021	3728621	EDMS-PSDB-3728621	na
8/27/2004	FDA Correspondence	na	Fax: Notice of Intent to Request Special Protocol Assessment: Carcinogenicity SN 021	na	na	3732055	EDMS-PSDB-3732055	na
9/2/2004	FDA Correspondence	na	Letter: IND Acknowledgement Letter	na	na	3776556	EDMS-PSDB-3776556	na
9/9/2004	IND Amendment	na	Briefing Package for 9/28/04 End of Phase 2 Meeting	na	022	3756672	EDMS-PSDB-3756672	na
10/1/2004	IND Amendment	na	Request for Special Protocol Assessment: Carcinogenicity Protocol	na	023	3810109	EDMS-PSDB-3810109	na
10/26/2004	IND Amendment	na	Follow-up Information for Request for Special Protocol Assessment: Carcinogenicity Protocol	na	024	3860095	EDMS-PSDB-3860095	na
10/26/2004	Record of Contact	9/28/2004	Minutes of the 9/28/04 End of Phase 2 FDA Meeting	na	na	3818660	EDMS-PSDB-3818660	na
10/26/2004	FDA Correspondence	na	Fax: 10/26/04 Submission SN 024	na	na	3928067	EDMS-PSDB-3928067	na
10/27/2004	General Correspondence	na	Minutes of the 9/28/04 End of Phase 2 Meeting and Post-Meeting Follow-up Information	na	025	3862824	EDMS-PSDB-3862824	na
10/28/2004	General Correspondence	na	Response to FDA Request in 10/12/04 End of Phase 2 CMC/Biopharm Meeting Minutes	na	026	3868773	EDMS-PSDB-3868773	na
11/9/2004	Protocol Amendment	na	New Protocol; New Investigator	R076477-PSY-3004	027	3902895	EDMS-PSDB-3902895	na
11/10/2004	General Correspondence	na	Request for a Type C Meeting	na	028	3907677	EDMS-PSDB-3907677	na
11/11/2004	Safety Report	na	US-JNJFOC-20041100394 Initial	R092670-SCH-704	029	3909784	EDMS-PSDB-3909784	na
11/15/2004	FDA Correspondence	na	Fax: Response to Carcinogenicity Protocol Assessment Request - Final CAC Report	na	na	3928113	EDMS-PSDB-3928113	na

Date	Submission Type	Date of Contact	Description	Protocol #	SN#	EDMS or Sequence #	Hyperlink	Gateway Report
11/18/2004	Information Amendment	na	CMC	na	030	3928878	EDMS-PSDB-3928878	na
11/22/2004	Safety Report	na	US-JNJFOC-20041102371 Initial	R076477-SCH-304	031	3931421	EDMS-PSDB-3931421	na
11/23/2004	Safety Report	na	US-JNJFOC-20041103584 Initial	R076477-SCH-304	032	3938295	EDMS-PSDB-3938295	na
11/23/2004	Safety Report	na	Fax: Safety report SN 032	R076477-SCH-304	na	3961743	EDMS-PSDB-3961743	na
11/23/2004	FDA Correspondence	na	US-JNJFOC-20041102371 F-1	R076477-SCH-304	033	3949874	EDMS-PSDB-3949874	na
11/30/2004	Safety Report	na	Pharmacology/Toxicology: Clinical	na	034	3955196	EDMS-PSDB-3955196	na
11/30/2004	Information Amendment	na	US-JNJFOC-20041103584 F-1	R076477-SCH-304	035	3961376	EDMS-PSDB-3961376	na
12/2/2004	Safety Report	na	MY-JNJFOC-20041105754 Initial	R076477-SCH-705	036	3963269	EDMS-PSDB-3963269	na
12/3/2004	Safety Report	na	Pharmacology/Toxicology	na	037	3967273	EDMS-PSDB-3967273	na
12/7/2004	Information Amendment	na	US-JNJFOC-20041201617 Initial	R076477-SCH-701	038	3976131	EDMS-PSDB-3976131	na
12/10/2004	Safety Report	na	IN-JNJFOC-20041202092 Initial	R076477-SCH-703	039	3998127	EDMS-PSDB-3998127	na
12/20/2004	Safety Report	na	Briefing Package for 1/13/05 Meeting	na	040	3998804	EDMS-PSDB-3998804	na
12/20/2004	General Correspondence	na	CA-JNJFOC-20041204345 Initial	R076477-SCH-305	041	4008929	EDMS-PSDB-4008929	na
12/23/2004	Safety Report	na	MY-JNJFOC-20041105754 F-1	R076477-SCH-705	042	4007899	EDMS-PSDB-4007899	na
12/23/2004	Safety Report	na	MY-JNJFOC-20041204460 Initial	R076477-SCH-705	043	4010952	EDMS-PSDB-4010952	na
12/27/2004	Safety Report	na	IN-JNJFOC-20041202092 F-1	R076477-SCH-703	044	4010959	EDMS-PSDB-4010959	na
12/27/2004	Safety Report	na	MY-JNJFOC-20041105754 F-2	R076477-SCH-705	045	4010966	EDMS-PSDB-4010966	na
12/27/2004	Safety Report	na	CA-JNJFOC-20041204345 F-1	R076477-SCH-305	046	4019867	EDMS-PSDB-4019867	na
1/4/2005	Safety Report	na	New Protocol: New Investigator	R092670-PSY-3001	047	4023920	EDMS-PSDB-4023920	na
1/6/2005	Protocol Amendment	na	MY-JNJFOC-20041105754 F-3	R076477-SCH-705	048	4026257	EDMS-PSDB-4026257	na
1/7/2005	Safety Report	na	US-JNJFOC-20041100394 F-1	R076477-SCH-704	049	4042911	EDMS-PSDB-4042911	na
1/14/2005	Safety Report	na	Pharmacology/Toxicology	na	050	4050521	EDMS-PSDB-4050521	na
1/18/2005	Information Amendment	na	PL-JNJFOC-20041206244 Initial	R076477-SCH-703	051	4050379	EDMS-PSDB-4050379	na
1/18/2005	Safety Report	na	US-JNJFOC-20050103392 Initial	R076477-SCH-701	052	4056138	EDMS-PSDB-4056138	na
1/19/2005	Safety Report	na	Fax: Safety Report SN 052	R076477-SCH-701	na	4063491	EDMS-PSDB-4063491	na
1/19/2005	FDA Correspondence	na	US-JNJFOC-20050103392 F-1	R076477-SCH-701	053	4063195	EDMS-PSDB-4063195	na
1/21/2005	Safety Report	na	CA-JNJFOC-20041204345 F-2	R076477-SCH-305	054	4066354	EDMS-PSDB-4066354	na
1/24/2005	Safety Report	na	US-JNJFOC-20050103392 F-2	R076477-SCH-301	055	4070650	EDMS-PSDB-4070650	na
1/26/2005	Safety Report	na	US-JNJFOC-20050105338 Initial	R076477-SCH-305	056	4092677	EDMS-PSDB-4092677	na
2/2/2005	Safety Report	na	New Investigators	R092670-PSY-3004	057	4093088	EDMS-PSDB-4093088	na
2/2/2005	Protocol Amendment	na	IN-JNJFOC-20041202092 F-2	R076477-SCH-703	058	4094614	EDMS-PSDB-4094614	na
2/3/2005	Safety Report	na	US-JNJFOC-20041100394 F-2	R076477-SCH-704	059	4098820	EDMS-PSDB-4098820	na
2/4/2005	Safety Report	na	MY-JNJFOC-20050105402 Initial	R076477-SCH-305	060	4098827	EDMS-PSDB-4098827	na
2/4/2005	Safety Report	na	RO-JNJFOC-20050201375 Initial	R076477-SCH-301	061	4115429	EDMS-PSDB-4115429	na
2/11/2005	Safety Report	na	Fax: Safety Report SN 061	R076477-SCH-301	na	4140901	EDMS-PSDB-4140901	na
2/11/2005	FDA Correspondence	na	US-JNJFOC-20050105338 F-1	R076477-SCH-305	062	4119644	EDMS-PSDB-4119644	na
2/14/2005	Safety Report	na	MY-JNJFOC-20050105402 F-1	R076477-SCH-305	063	4128519	EDMS-PSDB-4128519	na
2/17/2005	Safety Report	na	RO-JNJFOC-20050201375 F-1	R076477-SCH-301	064	4137747	EDMS-PSDB-4137747	na
2/22/2005	Safety Report	na	US-JNJFOC-20050304957 Initial	R076477-SCH-1009	065	4209442	EDMS-PSDB-4209442	na
3/23/2005	Safety Report	na	Fax: Safety Report SN 065	R076477-SCH-1009	na	4210799	EDMS-PSDB-4210799	na
3/23/2005	General Correspondence	na	US-JNJFOC-20050304957 F-1	R076477-SCH-1009	066	4224908	EDMS-PSDB-4224908	na
3/31/2005	Safety Report	na	TW-JNJFOC-20050305349 Initial	R076477-SCH-305	067	4233955	EDMS-PSDB-4233955	na
4/4/2005	Safety Report	na	MY-JNJFOC-20041204460 F-1	R076477-SCH-705	068	4255811	EDMS-PSDB-4255811	na
4/13/2005	Safety Report	na	MY-JNJFOC-20041204460 F-2	R076477-SCH-705	069	4259582	EDMS-PSDB-4259582	na
4/15/2005	Safety Report	na	NL-JNJFOC-20050402753 Initial	PALIOROS-SCH-1011	070	4267510	EDMS-PSDB-4267510	na
4/15/2005	Safety Report	na	Fax: Safety Report SN 070	PALIOROS-SCH-1011	na	4278984	EDMS-PSDB-4278984	na
4/15/2005	General Correspondence	na	US-JNJFOC-20050105338 F-2	R076477-SCH-305	071	4279747	EDMS-PSDB-4279747	na
4/20/2005	Safety Report	na	MY-JNJFOC-20041105754 F-4	R076477-SCH-705	072	4279761	EDMS-PSDB-4279761	na
4/20/2005	Safety Report	na	US-JNJFOC-20041100394 F-3	R076477-SCH-704	073	4279122	EDMS-PSDB-4279122	na
4/20/2005	Safety Report	na	NL-JNJFOC-20050402753 F-1	PALIOROS-SCH-1011	074	4287661	EDMS-PSDB-4287661	na
5/9/2005	IND Amendment	na	Reclassification of IND Safety Reports	na	075	4322913	EDMS-PSDB-4322913	na
5/9/2005	Protocol Amendment	na	New Protocol: New Investigator	R092670-PSY-3003	076	4322769	EDMS-PSDB-4322769	na

IND 67,356 (JNJ 16977831) (R092670) paliperidone palmitate

Date	Submission Type	Date of Contact	Description	Protocol #	SN#	EDMS or Sequence #	Hyperlink	Gateway Receipt
5/10/2005	Protocol Amendment	na	New Investigators	R092670-PSY-3004	077	4325611	EDMS-PSDB-4325611	na
5/11/2005	Protocol Amendment	na	New Investigators	R092670-PSY-3004	078	4329282	EDMS-PSDB-4329282	na
5/16/2005	Safety Report	na	US-JNJFOC-20050502821 Initial	R076477-SCH-1009	079	4343153	EDMS-PSDB-4343153	na
5/16/2005	FDA Correspondence	na	Fax: Safety Report SN 079	R076477-SCH-1009	na	4348879	EDMS-PSDB-4348879	na
5/23/2005	Safety Report	na	MY-JNJFOC-20041204460 F-3	R076477-SCH-705	080	4354981	EDMS-PSDB-4354981	na
5/25/2005	Safety Report	na	IN-JNJFOC-20050503897 Initial	R076477-SCH-301	081	4362170	EDMS-PSDB-4362170	na
5/25/2005	Safety Report	na	IN-JNJFOC-20050503897 F-1	R076477-SCH-301	082	4381574	EDMS-PSDB-4381574	na
6/10/2005	Information Amendment	na	CM&C	R092670-PSY-3003	083	4403047	EDMS-PSDB-1103047	na
6/13/2005	General Correspondence	na	Request for Review of Drug Product Registration Stability Protocol	na	084	4411495	EDMS-PSDB-4411495	na
6/14/2005	Information Amendment	na	Change in Protocol	R092670-PSY-3001	085	4411736	EDMS-PSDB-4411736	na
6/14/2005	Information Amendment	na	Change in Protocol	R092670-PSY-3004	086	4411745	EDMS-PSDB-4411745	na
6/15/2005	Information Amendment	na	New Protocol; New Investigators	R092670-PSY-3005	087	4416120	EDMS-PSDB-4416120	na
6/15/2005	Information Amendment	na	New Protocol; New Investigators	R092670-PSY-1001	088	4414564	EDMS-PSDB-4414564	na
6/15/2005	Safety Report	na	NL-JNJFOC-20050402753 F-2	PALIOROS-P01-1011	089	4421835	EDMS-PSDB-4421865	na
6/16/2005	Safety Report	na	US-JNJFOC-20041201617 F-1	R076477-SCH-301	090	4424386	EDMS-PSDB-4424386	na
6/17/2005	Safety Report	na	US-JNJFOC-20050103392 F-3	R076477-SCH-301	091	4431011	EDMS-PSDB-4431011	na
6/23/2005	Safety Report	na	US-JNJFOC-20050603607 Initial	R076477-SCH-705	092	4441911	EDMS-PSDB-4441911	na
6/28/2005	Protocol Amendment	na	New Protocol; New Investigators	R092670-PSY-1004	093	4460769	EDMS-PSDB-4460769	na
6/29/2005	Protocol Amendment	na	New Investigators	R092670-PSY-1004	094	4465586	EDMS-PSDB-4465586	na
7/1/2005	Safety Report	na	US-JNJFOC-20050304957 F-2	R076477-SCH-1009	095	4477198	EDMS-PSDB-4477198	na
7/6/2005	Safety Report	na	IN-JNJFOC-20050503897 F-2	R076477-SCH-301	096	4482015	EDMS-PSDB-4482015	na
7/6/2005	Safety Report	na	US-JNJFOC-20050603607 F-1	R076477-SCH-705	097	4484198	EDMS-PSDB-4484198	na
7/15/2005	Safety Report	na	MY-JNJFOC-20041204460 F-4	R076477-SCH-705	098	4520333	EDMS-PSDB-4520333	na
7/19/2005	IND Amendment	na	Investigator's Brochure: Agenda	na	099	4525548	EDMS-PSDB-4525548	na
7/20/2005	Safety Report	na	CM&C	R076477-SCH-705	100	4529100	EDMS-PSDB-4529100	na
7/20/2005	Information Amendment	na	Request for Review of Revised Drug Product Registration	na	101	4531527	EDMS-PSDB-4531527	na
7/26/2005	Protocol Amendment	na	Stability Protocol	R092670-PSY-1002	102	4544136	EDMS-PSDB-4544136	na
8/1/2005	IND Amendment	na	Stability Protocol	na	103	4565568	EDMS-PSDB-4565568	na
8/5/2005	Annual Report	na	Reporting Period: 06/07/04 - 06/06/05	na	104	4574605	EDMS-PSDB-4574605	na
8/5/2005	Protocol Amendment	na	New Protocol; New Investigators	R092670-PSY-1002	105	4586146	EDMS-PSDB-4586146	na
9/9/2005	Record of Contact	na	FDA Acceptance of Amended Drug Production Registration	na	na	4692158	EDMS-PSDB-4692158	na
9/26/2005	FDA Correspondence	na	Stability Protocol for F013	R092670-PSY-3004	na	4758438	EDMS-PSDB-4758438	na
9/27/2005	Record of Contact	9/26/2005	Fax: Report to FDA from Sterling IRB Report Received from Sterling IRB Regarding CBH Health LLC	na	na	4821292	EDMS-PSDB-4821292	na
9/29/2005	General Correspondence	na	J. Martynowicz is Now Primary Contact	na	106	4762944	EDMS-PSDB-4762944	na
9/30/2005	Protocol Amendment	na	New Investigators	R092670-PSY-1004	107	4764829	EDMS-PSDB-4764829	na
9/30/2005	Protocol Amendment	na	New Investigators	R092670-PSY-3004	108	4771325	EDMS-PSDB-4771325	na
10/26/2005	Safety Report	na	RO-JNJFOC-20050201375 F-2	R076477-SCH-301	109	4867147	EDMS-PSDB-4867147	na
11/11/2005	Safety Report	na	CA-JNJFOC-20051101512 Initial	R076477-SCH-705	110	4925304	EDMS-PSDB-4925304	na
11/21/2005	Safety Report	na	Request for Review of Revised Drug Product Registration	na	111	4951293	EDMS-PSDB-4951293	na
11/29/2005	IND Amendment	na	Stability Protocol	na	112	4966845	EDMS-PSDB-4966845	na
12/20/2005	Record of Contact	12/7/2005	Minutes of the 12/7/05 Bipolar I Disorder End-of-Phase 2/Pre-Phase 3 Meeting	na	na	5019672	EDMS-PSDB-5019672	na
12/21/2005	General Correspondence	na	Minutes of the 12/7/05 End of Phase 2 Meeting	na	113	5029714	EDMS-PSDB-5029714	na
12/22/2005	Safety Report	na	CA-JNJFOC-20051101512 F-2	R076477-SCH-705	114	5030729	EDMS-PSDB-5030729	na
12/29/2005	Safety Report	na	CA-JNJFOC-20051101512 F-3	R076477-SCH-705	115	5040289	EDMS-PSDB-5040289	na
2/2/2006	Protocol Amendment	na	New Protocol; New Investigators	R092670-PSY-3002	116	5131076	EDMS-PSDB-5131076	na
2/23/2006	Protocol Amendment	na	New Investigators	R092670-PSY-3004	117	5205422	EDMS-PSDB-5205422	na

Date	Submission Type	Date of Contact	Description	Protocol #	SN#	EDMS or Sequence #	Hyperlink	Gateway Receipt
3/6/2006	General Correspondence	na	IRB Waiver Request	na	118	5248420	EDMS-PSDB-5248420	na
3/24/2006	Safety Report	na	IN-JNJFOC-20060205306 7/15 Day Initial	R076477-SCH-701	119	5324478	EDMS-PSDB-5324478	na
3/24/2006	General Correspondence	na	Fax: IN-JNJFOC-20060205306 7/15 Day Initial	R076477-SCH-701	119	5358805	EDMS-PSDB-5358805	na
3/27/2006	Information Amendment	na	Clinical: Statistical Analysis Plan for R092670-PSY-3004	R092670-PSY-3004	120	5330146	EDMS-PSDB-5330146	na
4/3/2006	General Correspondence	na	Fax: IN-JNJFOC-20060205306 7/15 Day F-1	R076477-SCH-701	121	5352966	EDMS-PSDB-5352966	na
5/26/2006	FDA Correspondence	na	Letter: IRB Waiver Request Granted (S-117)	R092670-PSY-3004	na	5546925	EDMS-PSDB-5546925	na
5/26/2006	FDA Correspondence	na	Email/Attachment: IRB Waiver Request Granted (S-117)	R092670-PSY-3004	na	5545009	EDMS-PSDB-5545009	na
6/20/2006	IND Amendment	na	Protocol R092670-PSY-3003 Medication Kit Error	R092670-PSY-3003	122	5593354	EDMS-PSDB-5593354	na
6/26/2006	Information Amendment	na	Clinical: Statistical Analysis Plan for R092670-PSY-3003	R092670-PSY-3003	123	5617192	EDMS-PSDB-5617192	na
6/27/2006	Record of Contact	6/23/2006	DSI Notification of Study Compliance Deficiencies	na	na	6380254	EDMS-PSDB-6380254	na
7/11/2006	Information Amendment	na	Clinical	R092670-PSY-3001; R092670-PSY-3002; R092670-PSY-1004	124	5645851	EDMS-PSDB-5645851	na
7/12/2006	Safety Report	na	IN-JNJFOC-20060205306 F-2	R076477-SCH-701	125	5662755	EDMS-PSDB-5662755	na
7/17/2006	FDA Correspondence	na	Email/Attachment: Poland Investigator Site Audit with CL for SN 124	R092670-PSY-3001; R092670-PSY-3002; R092670-PSY-1004	na	5704533	EDMS-PSDB-5704533	na
7/21/2006	FDA Correspondence	na	Email: SAP for R092670-PSY-3003	R092670-PSY-3003	na	5714883	EDMS-PSDB-5714883	na
7/31/2006	FDA Correspondence	na	Email: FDA Response to Statistical Questions from 6/26/06	na	na	6033820	EDMS-PSDB-6033820	na
8/10/2006	IND Amendment	na	Investigator's Brochure: Addendum	na	126	5755623	EDMS-PSDB-5755623	na
8/14/2006	IND Amendment	na	Gen Corr: Request for Type B Pre-Phase 3 Meeting	na	127	5765064	EDMS-PSDB-5765064	na
8/17/2006	FDA Correspondence	na	Email: Secure E-Mail	na	na	5799979	EDMS-PSDB-5799979	na
9/1/2006	IND Amendment	na	Gen Corr: Request for Type C Meeting	na	128	5827016	EDMS-PSDB-5827016	na
9/6/2006	Safety Report	na	IN-JNJFOC-20060805629 Initial	R076477-BIM-3002	129	5838723	EDMS-PSDB-5838723	na
9/12/2006	FDA Correspondence	na	Email/Attachment: Meeting Request	na	na	5922314	EDMS-PSDB-5922314	na
9/18/2006	Annual Report	na	Reporting Period: 06/07/05 - 06/06/06	na	130	5868840	EDMS-PSDB-5868840	na
9/20/2006	FDA Correspondence	na	Email: Electronic Submissions	na	na	5922383	EDMS-PSDB-5922383	na
9/21/2006	General Correspondence	na	Request for Special Protocol Assessment	R076477-SCA-3003	131	5895887	EDMS-PSDB-5895887	na
9/22/2006	FDA Correspondence	na	Email: Meeting Granted	na	na	5922505	EDMS-PSDB-5922505	na
9/22/2006	FDA Correspondence	na	Email: Bipolar & Schizophrenia Meeting Requests	na	na	5922449	EDMS-PSDB-5922449	na
9/25/2006	FDA Correspondence	na	Email: Bipolar & Schizophrenia Meeting Requests	na	na	5922559	EDMS-PSDB-5922559	na
9/26/2006	FDA Correspondence	na	Email: Meeting Granted (12:08pm)	na	na	5922643	EDMS-PSDB-5922643	na
9/26/2006	FDA Correspondence	na	Email: Meeting Granted (3:22pm)	na	na	5922614	EDMS-PSDB-5922614	na
9/26/2006	Safety Report	na	IN-JNJFOC-20060805629 F-1	R076477-BIM-3002	132	5908836	EDMS-PSDB-5908836	na
10/6/2006	General Correspondence	na	eCTD Submission Conversion	na	133	0000	GW eCTD TOC	na
10/11/2006	Safety Report	na	IN-JNJFOC-20060205306 7/15 Day F-3	R076477-SCH-701	134	0134	GW eCTD TOC	na
10/18/2006	Safety Report	na	IN-JNJFOC-20060805629 F-2	R076477-BIM-3002	135	0135	GW eCTD TOC	na
10/27/2006	FDA Correspondence	na	Email: Transfer of Regulatory Responsibility	na	na	6027759	EDMS-PSDB-6027759	na
11/3/2006	FDA Correspondence	na	Letter: RFI in Response to 9/21/06 Request for Special Protocol Assessment	na	na	6058010	EDMS-PSDB-6058010	na
11/6/2006	Information Amendment	na	Clinical: Statistical Analysis Plan for PSY-3001	R092670-PSY-3001	136	0136	GW eCTD TOC	na
11/9/2006	General Correspondence	na	Briefing Pkg. For 12/11/06 Type C Meeting	na	137	0137	GW eCTD TOC	na
11/27/2006	Safety Report	na	IN-JNJFOC-20060805629 F-3	R076477-BIM-3002	138	0138	GW eCTD TOC	na
12/4/2006	FDA Correspondence	na	Email: N136 Stats Comments	na	na	6159463	EDMS-PSDB-6159463	na
12/7/2006	FDA Correspondence	na	Email/Attachment: N136 Stats Comments	R092670-PSY-3001	na	6163931	EDMS-PSDB-6163931	na
12/8/2006	Safety Report	na	SE-JNJFOC-20061005337 1	R092670-PSY-3002	139	0139	GW eCTD TOC	na
12/18/2006	Safety Report	na	Multiple (9)	Multiple	140	0140	GW eCTD TOC	na
12/18/2006	Safety Report	na	DE-JNJFOC-20061200532 1	R076477-BIM-3004	141	0141	GW eCTD TOC	na
12/19/2006	Information Amendment	na	Clinical: Statistical Analysis Plan for R092670-PSY-3001	R092670-PSY-3001	142	0142	GW eCTD TOC	na
12/21/2006	Record of Contact	12/11/2006	Minutes from the Meeting with the FDA Division of Psychiatry Products on 12/11/06	na	na	6218032	EDMS-PSDB-6218032	na
12/22/2006	Protocol Amendment	na	Statistical Analysis Plan for R092670-PSY-3005	R092670-PSY-3005	143	0143	GW eCTD TOC	na

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12/27/2006	IND Amendment	na	Minutes of December 11, 2006 Type C Meeting	na	144	0144	GW eCTD TOC	na
12/29/2006	FDA Correspondence	na	Letter: Official Meeting Minutes from 12/11/06 Telecon	na	na	6248267	EDMS-PSDB-6248267	na
1/3/2007	FDA Correspondence	na	Email/Attachment: Official Meeting Minutes from 12/11/06 Telecon	na	na	6241885	EDMS-PSDB-6241885	na
1/4/2007	Protocol Amendment	na	New Protocol	R092670-PSY-3007	145	0145	GW eCTD TOC	na
1/9/2007	General Correspondence	na	Request for Type B Pre-Phase 3 Meeting	na	146	0146	GW eCTD TOC	na
1/9/2007	FDA Correspondence	na	Email/Attachment: Meeting Request, Paliperidone Palmitate Bipolar Development Program	na	na	6264901	EDMS-PSDB-6264901	na
1/19/2007	FDA Correspondence	na	Email: Plan to Stop Study R092670-PSY-3001	R092670-PSY-3001	na	6308521	EDMS-PSDB-6308521	na
1/23/2007	Record of Contact	na	FDA Div. Of Scientific Affairs: Telephone Contact Memo Between FDA and Local Trial Manager in Global Clinical Operations	R092670-PSY-3001	na	6360613	EDMS-PSDB-6360613	na
1/24/2007	General Correspondence	na	Response to RFI: Copy of Protocol R092670-PSY-3001	R092670-PSY-3001	na	6324934	EDMS-PSDB-6324934	na
1/26/2007	Protocol Amendment	na	Notification of PSY-3001 Study Termination Due to Efficacy; Change in Protocol R092670-PSY-3001; Final Statistical Analysis Plan for R092670-PSY-3001	R092670-PSY-3001	147	0147	GW eCTD TOC	na
1/31/2007	General Correspondence	na	IRB Waiver Request	R092670-PSY-3007	148	0148	GW eCTD TOC	na
2/2/2007	Protocol Amendment	na	New Protocol; New Investigators	R092670-PSY-3006	149	0149	GW eCTD TOC	na
2/6/2007	IND Amendment	na	IRB Waiver Request	R092670-PSY-3006	150	0150	GW eCTD TOC	na
2/11/2007	Record of Contact	2/6/2007	GCP Violations at Dr. Chaganli's Site Under Protocol R092670-PSY-3001	R092670-PSY-3001	na	6383191	EDMS-PSDB-6383191	na
2/12/2007	General Correspondence	na	Response to RFI from DS: Protocol R092670-PSY-3001 Site Closure: MedClin Research, Inc.	R092670-PSY-3001	151	0151	GW eCTD TOC	na
2/15/2007	Safety Report	na	US-JNJFOC-20070201813 Initial	R076477-SCA-3002	152	0152	GW eCTD TOC	na
2/16/2007	General Correspondence	na	Request for a Type B, Pre-NDA Meeting	na	153	0153	GW eCTD TOC	na
2/16/2007	FDA Correspondence	na	Fax/Attachment: 7/15 Day Safety Report (K Kiedrow)	na	154	6416129	EDMS-PSDB-6416129	na
2/16/2007	FDA Correspondence	na	Fax/Attachment: 7/15 Day Safety Report (D Bates)	na	154	6415933	EDMS-PSDB-6415933	na
2/16/2007	Safety Report	na	US-JNJFOC-20070203055 Initial 7/15 Day Report	R076477-BIM-3004	154	154	GW eCTD TOC	na
2/22/2007	FDA Correspondence	na	Email: 4/18/07 Type B Meeting Request Granted	na	na	6429676	EDMS-PSDB-6429676	na
2/26/2007	Safety Report	na	US-JNJFOC-20070204832 Initial	R076477-SCA-3001	155	0155	GW eCTD TOC	na
2/26/2007	Safety Report	na	Fax: US-JNJFOC-20070204832 Initial	R076477-SCA-3001	155	6446121	EDMS-PSDB-6446121	na
2/26/2007	FDA Correspondence	na	Letter: IRB Waiver Granted for 2/16/07 SN 150 Submission	R092670-PSY-3006	na	6452312	EDMS-PSDB-6452312	na
2/26/2007	FDA Correspondence	na	Letter: IRB Waiver Granted for 1/31/07 SN 148 Submission	R092670-PSY-3007	na	6526103	EDMS-PSDB-6526103	na
2/28/2007	Safety Report	na	US-JNJFOC-20070203055 F-1	R076477-BIM-3004	156	0156	GW eCTD TOC	na
3/5/2007	Safety Report	na	US-JNJFOC-20070204832 F-1	R076477-SCA-3001	157	0157	GW eCTD TOC	na
3/8/2007	Protocol Amendment	na	New Investigator	R092670-PSY-3007	158	0158	GW eCTD TOC	na
3/9/2007	Protocol Amendment	na	New Investigator	R092670-PSY-3006	159	0159	GW eCTD TOC	na
3/15/2007	IND Amendment	na	Briefing Package for 4/18/07 Type B Pre-NDA Meeting	na	160	0160	GW eCTD TOC	na
3/20/2007	Safety Report	na	US-JNJFOC-20070204832 F-2	R076477-SCA-3001	161	0161	GW eCTD TOC	na
3/22/2007	Protocol Amendment	na	Change in Protocol and Statistical Analysis Plan	R092670-PSY-3002	162	0162	GW eCTD TOC	na
3/26/2007	General Correspondence	na	Request for a Type B CMC/BioPharmaceutics Pre-NDA Meeting	na	163	0163	GW eCTD TOC	na
3/28/2007	Information Amendment	na	Clinical	na	164	0164	GW eCTD TOC	na
3/30/2007	Protocol Amendment	na	New and Updated Investigators	R092670-PSY-3007	165	0165	GW eCTD TOC	na
3/30/2007	FDA Correspondence	na	Email: Request for Submission Information	na	na	6614450	EDMS-PSDB-6614450	na
4/5/2007	FDA Correspondence	na	Email: SN 162 SAP - Question about Submission Study	R092670-PSY-3002	na	6637219	EDMS-PSDB-6637219	na
4/6/2007	General Correspondence	na	Response to FDA RFI: Additional Safety Information	na	166	0166	GW eCTD TOC	na
4/9/2007	FDA Correspondence	na	Email: Reply to FDS's 4/5/07 Study Question	R092670-PSY-3002	na	6637270	EDMS-PSDB-6637270	na
4/11/007	FDA Correspondence	na	Email: S162 SAP	na	na	na	04-11-07 Email	na
4/16/2007	Safety Report	na	RO-JNJFOC-20060503643 F-1	R092670-PSY-3001	167	0167	GW eCTD TOC	na
4/17/2007	Safety Report	na	US-JNJFOC-20070203055 F-2	R076477-BIM-3004	168	0168	GW eCTD TOC	na
4/19/2007	Safety Report	na	US-JNJFOC-20070401462 Initial	R076477-BIM-3002	169	0169	GW eCTD TOC	na

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4/24/2007	FDA Correspondence	na	Email: Meeting Granted & Request for Meeting Pkg. By 5/10/07 S/163	na	na	6733756	EDMS-PSDB-6733756	na
4/25/2007	Safety Report	na	DE-JNJFOC-20061200532 F-1	R076477-BIM-3004	170	0170	GW eCTD TOC	na
4/30/2007	Safety Report	na	US-JNJFOC-20070405377 7-Day Initial	R076477-BIM-3004	171	0171	GW eCTD TOC	na
4/30/2007	FDA Correspondence	na	Fax: SN 171	na	na	6793658	EDMS-PSDB-6793658	na
4/30/2007	FDA Correspondence	na	Fax: SN 171 (2nd sending of fax)	na	na	6793660	EDMS-PSDB-6793660	na
5/3/2007	FDA Correspondence	na	Letter: 04/18/07 Official Meeting Minutes S/153	na	na	6801969	EDMS-PSDB-6801969	na
5/4/2007	Safety Report	na	US-JNJFOC-20070405377 7-Day F-1	R076477-BIM-3004	172	0172	GW eCTD TOC	na
5/4/2007	Safety Report	na	US-JNJFOC-20070404476 Initial	R076477-BIM-3001	173	0173	GW eCTD TOC	na
5/7/2007	Safety Report	na	US-JNJFOC-20070405377 7-Day F-2	R076477-BIM-3004	174	0174	GW eCTD TOC	na
5/8/2007	Safety Report	na	US-JNJFOC-20070404476 F-1	R076477-BIM-3001	175	0175	GW eCTD TOC	na
5/7/2007	FDA Correspondence	na	Email/Attachment: 04/18/07 Meeting Minutes S/153	na	na	6806260	EDMS-PSDB-6806260	na
5/9/2007	General Correspondence	na	Briefing Package for 6/7/07 CMC/BioPharmaceutics Type B pre-NDA Meeting	na	176	0176	GW eCTD TOC	na
5/9/2007	Safety Report	na	US-JNJFOC-20070204832 F-3	R076477-SCA-3001	177	0177	GW eCTD TOC	na
5/9/2007	FDA Correspondence	na	Letter: 1/4/07 SN 145 Statistical Review with Comments	R092670-PSY-3007	na	na	05-09-07 Letter	na
5/11/2007	General Correspondence	na	Minutes of the 4/18/07 Pre-NDA Meeting	na	178	0178	GW eCTD TOC	na
5/16/2007	Safety Report	na	US-JNJFOC20070201813 F-1	R076477-SCA-3002	179	0179	GW eCTD TOC	na
5/22/2007	Safety Report	na	US-JNJFOC-20070204832 F-4	R076477-SCA-3001	180	0180	GW eCTD TOC	na
5/24/2007	Protocol Amendment	na	Change in Protocol: New Investigators	R092670-PSY-3006	181	0181	GW eCTD TOC	na
5/25/2007	Information Amendment	na	Nonclinical Pharmacology Study Report	na	182	0182	GW eCTD TOC	na
6/4/2007	FDA Correspondence	na	Email/Attachment: Preliminary Comments for 6/7/07 Meeting	na	na	na	06-04-07 Email	na
6/8/2007	Record of Contact	6/8/2007	Protocol PSY-3001 "Rate" Qualifications	R092670-PSY-3001	na	6963412	EDMS-PSDB-6963412	na
6/8/2007	Protocol Amendment	na	Change in Protocol: New Investigators	R092670-PSY-3007	183	0183	GW eCTD TOC	na
6/14/2007	Protocol Amendment	na	New Protocol	R092670-PSY-1008	184	0184	GW eCTD TOC	na
6/15/2007	General Correspondence	na	IRB Waiver Request	R092670-PSY-1008	185	0185	GW eCTD TOC	na
6/15/2007	FDA Correspondence	na	Email: IND 67,356 3-Month Product Formulation: IND 76,952	na	na	na	06-15-07 Email	na
6/29/2007	FDA Correspondence	na	Letter: 06/07/07 Official Meeting Minutes	R092670-PSY-3006	186	0186	GW eSIG TOC	na
7/31/2007	Protocol Amendment	na	Change in Protocol	R092670-PSY-3007	187	0187	GW eSIG TOC	na
8/1/2007	Protocol Amendment	na	New Investigators	na	188	0188	GW eSIG TOC	na
8/13/2007	General Correspondence	na	Clarification of Official Minutes of the 07 June 2007 Meeting - CMC & BioPharmaceutics pre-NDA	na	na	na	na	na
8/21/2007	Safety Report	na	DE-JNJFOC-20061200532 F-2	R076477-BIM-3004	189	0189	GW eSIG TOC	na
8/27/2007	General Correspondence	na	Sample Dataset Submission for IT Testing	na	190	0190	GW eSIG TOC	na
9/12/2007	FDA Correspondence	na	Email: Paliperidone palmitate NDA Submission Plans	na	na	na	09-12-07 Email	na
9/19/2007	Protocol Amendment	na	Change in Protocol: New Investigators	R092670-PSY-1008	191	0191	GW eSIG TOC	na
9/20/2007	Annual Report	na	Reporting Period: 07/20/06 - 07/19/07	na	192	0192	GW eSIG TOC	na
11/1/2007	Protocol Amendment	na	New Investigators	R092670-PSY-3007	193	0193	GW eSIG TOC	na
11/2/2007	Protocol Amendment	na	New Investigators	R092670-PSY-3006	194	0194	GW eSIG TOC	na
11/29/2007	Safety Report	na	DE-JNJFOC-20061200532 F-3	R076477-BIM-3004	195	0195	GW eSIG TOC	na
12/6/2007	Record of Contact	6/16/2004	Minutes of June 16, 2004 CMC/BioPharmaceutics End of Phase 2 Meeting for Paliperidone Palmitate	na	na	na	12-06-07 Email	na
12/11/2007	Information Amendment	na	CMC Drug Substance, Drug Product and Stability Data	na	196	0196	GW eSIG TOC	na
12/21/2007	General Correspondence	na	Request for Proposed Proprietary Name Review	na	197	0197	GW eSIG TOC	na
12/27/2007	Protocol Amendment	na	New Investigators	R092670-PSY-3006	198	0198	GW eSIG TOC	na
1/9/2008	Information Amendment	na	Pharmacology/Toxicology	na	199	0199	GW eSIG TOC	na
1/15/2008	Protocol Amendment	na	New Investigators	R092670-PSY-3007	200	0200	GW eSIG TOC	na
1/23/2008	Protocol Amendment	na	Statistical Analysis Plan for R092670-PSY-3007	R092670-PSY-3007	201	0201	GW eSIG TOC	na
1/25/2008	General Correspondence	na	Postmarketing Study Commitment Final Report: Developmental Toxicity Study in the Rat Final Report	na	202	0202	GW eSIG TOC	na
1/30/2008	FDA Correspondence	na	Email/Attachment: IRB Waiver Granted	na	na	na	01-30-08 Email	na
2/1/2008	Protocol Amendment	na	New Investigators	R092670-PSY-1008	203	0203	GW eSIG TOC	na

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Date	Submission Type	Date of Contact	Description	Protocol #	SN#	EDMS of Sequence #	Hyperlink	Gateway Receipt
5/6/2003	Original IND	na	Original IND (50 Volumes)	na	000	Multiple	Original IND	na
5/13/2003	Record of Contact	5/13/2003	Request for Additional Desk Copies and IND Number for Paliperidone palmitate	na	na	2651976	EDMS-PSDB-2651976	na
5/19/2003	Record of Contact	5/19/2003	Request for List of Nonclinical Studies Submitted Under IND 67,356	na	na	2656702	EDMS-PSDB-2656702	na
5/28/2003	General Correspondence	na	Response to Request by Review Chemist	na	001	2676686	EDMS-PSDB-2676686	na
5/30/2003	General Correspondence	na	Response to Request from Dr. Lois Freed	na	002	2683477	EDMS-PSDB-2683477	na
6/2/2003	Record of Contact	6/2/2003	Clearance to Proceed with the Studies Under IND	na	na	2697285	EDMS-PSDB-2697285	na
6/5/2003	General Correspondence	na	Response to Request by Review Chemist	na	003	2716903	EDMS-PSDB-2716903	na
9/11/2003	Protocol Amendment	na	New Investigators	R092670-USA-3	004	2931978	EDMS-PSDB-2931978	na
9/12/2003	Information Amendment	na	CMC; Pharmacology/Toxicology	na	005	2937288	EDMS-PSDB-2937288	na
10/28/2003	Protocol Amendment	na	New Protocol; New Investigator	R092670-SCH-201	006	3044512	EDMS-PSDB-3044512	na
1/9/2004	Protocol Amendment	na	New Investigators	R092670-SCH-201	007	3195694	EDMS-PSDB-3195694	na
1/23/2004	Protocol Amendment	na	New Investigators	R092670-SCH-201	008	3230681	EDMS-PSDB-3230681	na
2/11/2004	Protocol Amendment	na	New Investigators	R092670-SCH-201	009	3288697	EDMS-PSDB-3288697	na
3/31/2004	Safety Report	na	US-JUNFOC-20040304794 Initial	R076477-SCH-304	010	3397560	EDMS-PSDB-3397560	na
4/22/2004	General Correspondence	na	Request for Type B End of Phase 2 Meeting - Chemistry, Microbiology, and Biopharmaceutics	na	011	3442328	EDMS-PSDB-3442328	na
4/29/2004	FDA Correspondence	na	Letter: Meeting Request Granted for 6/16/04	na	na	3548304	EDMS-PSDB-3548304	na
5/6/2004	General Correspondence	na	Request for a Type B End of Phase 2 Meeting	na	012	3474299	EDMS-PSDB-3474299	na
5/10/2004	Safety Report	na	US-JUNFOC-20040304794 F-1	R076477-SCH-304	013	3479851	EDMS-PSDB-3479851	na
5/20/2004	General Correspondence	na	Briefing Package for 6/16/04 CMC/Biopharm Meeting	na	014	3514273	EDMS-PSDB-3514273	na
6/16/2004	Record of Contact	6/16/2004	Minutes of 6/16/04 CMC/Biopharmaceutics End of Phase 2 Meeting for Paliperidone palmitate	na	na	3594054	EDMS-PSDB-3594054	na
6/28/2004	General Correspondence	na	Minutes of 6/16/04 Type B End of Phase 2 Meeting - CMC/Biopharmaceutics	na	015	3599384	EDMS-PSDB-3599384	na
7/11/2004	Protocol Amendment	na	New Investigators	R092670-SCH-201	016	3609437	EDMS-PSDB-3609437	na
8/4/2004	Annual Report	na	Reporting Period: 6/7/03 - 6/6/04	na	017	3681428	EDMS-PSDB-3681428	na
8/12/2004	Safety Report	na	IN-JUNFOC-20040800656 Initial	R076477-SCH-303	018	3699361	EDMS-PSDB-3699361	na
8/17/2004	Protocol Amendment	na	New Investigators	R092670-SCH-201	019	3704542	EDMS-PSDB-3704542	na
8/25/2004	Safety Report	na	IN-JUNFOC-20040800656 F-1	R076477-SCH-303	020	3723435	EDMS-PSDB-3723435	na
8/27/2004	General Correspondence	na	Notice of Intent to Request Special Protocol Assessment: Carcinogenicity	na	021	3728621	EDMS-PSDB-3728621	na
8/27/2004	FDA Correspondence	na	Fax: Notice of Intent to Request Special Protocol Assessment: Carcinogenicity SN 021	na	na	3732055	EDMS-PSDB-3732055	na
9/2/2004	FDA Correspondence	na	Letter: IND Acknowledgement Letter	na	na	3776556	EDMS-PSDB-3776556	na
9/9/2004	IND Amendment	na	Briefing Package for 9/28/04 End of Phase 2 Meeting	na	022	3756672	EDMS-PSDB-3756672	na
10/1/2004	IND Amendment	na	Request for Special Protocol Assessment: Carcinogenicity Protocol	na	023	3810109	EDMS-PSDB-3810109	na
10/26/2004	IND Amendment	na	Follow-up Information for Request for Special Protocol Assessment: Carcinogenicity Protocol	na	024	3860095	EDMS-PSDB-3860095	na
10/26/2004	Record of Contact	9/28/2004	Minutes of the 9/28/04 End of Phase 2 FDA Meeting	na	na	3818660	EDMS-PSDB-3818660	na
10/26/2004	FDA Correspondence	na	Fax: 10/26/04 Submission SN 024	na	na	3928067	EDMS-PSDB-3928067	na
10/27/2004	General Correspondence	na	Minutes of the 9/28/04 End of Phase 2 Meeting and Post-Meeting Follow-up Information	na	025	3862824	EDMS-PSDB-3862824	na
10/28/2004	General Correspondence	na	Response to FDA Request in 10/12/04 End of Phase 2 CMC/Biopharm Meeting Minutes	na	026	3868773	EDMS-PSDB-3868773	na
11/9/2004	Protocol Amendment	na	New Protocol: New Investigator	R076477-PSY-3004	027	3902895	EDMS-PSDB-3902895	na
11/10/2004	General Correspondence	na	Request for a Type C Meeting	na	028	3907677	EDMS-PSDB-3907677	na
11/11/2004	Safety Report	na	US-JUNFOC-20041100394 Initial	R092670-SCH-704	029	3909784	EDMS-PSDB-3909784	na
11/15/2004	FDA Correspondence	na	Fax: Response to Carcinogenicity Protocol Assessment Request - Final CAC Report	na	na	3928113	EDMS-PSDB-3928113	na

Date	Submission Type	Date of Contact	Description	Protocol #	SN#	EDMS or Sequence #	Hyperlink	Gateway Receipt
11/18/2004	Information Amendment	na	CMC	na	030	3928878	EDMS-PSDB-3928878	na
11/22/2004	Safety Report	na	US-JNJFOC-20041102371 Initial	R076477-SCH-304	031	3931421	EDMS-PSDB-3931421	na
11/23/2004	Safety Report	na	US-JNJFOC-20041103584 Initial	R076477-SCH-304	032	3938295	EDMS-PSDB-3938295	na
11/23/2004	FDA Correspondence	na	Fax: Safety report SN 032	R076477-SCH-304	na	3961743	EDMS-PSDB-3961743	na
11/30/2004	Safety Report	na	US-JNJFOC-20041102371 F-1	R076477-SCH-304	033	3949874	EDMS-PSDB-3949874	na
11/30/2004	Information Amendment	na	Pharmacology/Toxicology: Clinical	na	034	3955196	EDMS-PSDB-3955196	na
12/2/2004	Safety Report	na	US-JNJFOC-20041103584 F-1	R076477-SCH-304	035	3961376	EDMS-PSDB-3961376	na
12/3/2004	Safety Report	na	MY-JNJFOC-20041105754 Initial	R076477-SCH-705	036	3963269	EDMS-PSDB-3963269	na
12/7/2004	Information Amendment	na	Pharmacology/Toxicology	na	037	3967273	EDMS-PSDB-3967273	na
12/10/2004	Safety Report	na	US-JNJFOC-20041201617 Initial	R076477-SCH-701	038	3976131	EDMS-PSDB-3976131	na
12/20/2004	Safety Report	na	US-JNJFOC-20041202092 Initial	R076477-SCH-703	039	3998127	EDMS-PSDB-3998127	na
12/20/2004	General Correspondence	na	Briefing Package for 1/13/05 Meeting	na	040	3998804	EDMS-PSDB-3998804	na
12/23/2004	Safety Report	na	CA-JNJFOC-20041204345 Initial	R076477-SCH-705	041	4008929	EDMS-PSDB-4008929	na
12/23/2004	Safety Report	na	MY-JNJFOC-20041105754 F-1	R076477-SCH-705	042	4007899	EDMS-PSDB-4007899	na
12/27/2004	Safety Report	na	MY-JNJFOC-20041204460 Initial	R076477-SCH-703	043	4010952	EDMS-PSDB-4010952	na
12/27/2004	Safety Report	na	IN-JNJFOC-20041202092 F-1	R076477-SCH-705	044	4010959	EDMS-PSDB-4010959	na
12/27/2004	Safety Report	na	MY-JNJFOC-20041105754 F-2	R076477-SCH-705	045	4010966	EDMS-PSDB-4010966	na
1/4/2005	Safety Report	na	CA-JNJFOC-20041204345 F-1	R076477-SCH-305	046	4019867	EDMS-PSDB-4019867	na
1/6/2005	Protocol Amendment	na	New Protocol: New Investigator	R092670-PSY-3001	047	4023920	EDMS-PSDB-4023920	na
1/7/2005	Safety Report	na	MY-JNJFOC-20041105754 F-3	R076477-SCH-705	048	4026257	EDMS-PSDB-4026257	na
1/14/2005	Safety Report	na	US-JNJFOC-20041100394 F-1	R076477-SCH-704	049	4042911	EDMS-PSDB-4042911	na
1/18/2005	Information Amendment	na	Pharmacology/Toxicology	na	050	4050521	EDMS-PSDB-4050521	na
1/18/2005	Safety Report	na	PL-JNJFOC-20041206244 Initial	R076477-SCH-703	051	4050379	EDMS-PSDB-4050379	na
1/19/2005	Safety Report	na	US-JNJFOC-20050103392 Initial	R076477-SCH-701	052	4056138	EDMS-PSDB-4056138	na
1/19/2005	FDA Correspondence	na	Fax: Safety Report SN 032	R076477-SCH-701	na	4063491	EDMS-PSDB-4063491	na
1/21/2005	Safety Report	na	US-JNJFOC-20050103392 F-1	R076477-SCH-701	053	4063195	EDMS-PSDB-4063195	na
1/24/2005	Safety Report	na	CA-JNJFOC-20041204345 F-2	R076477-SCH-305	054	4066354	EDMS-PSDB-4066354	na
1/26/2005	Safety Report	na	US-JNJFOC-20050103392 F-2	R076477-SCH-301	055	4070650	EDMS-PSDB-4070650	na
2/2/2005	Safety Report	na	US-JNJFOC-20050103338 Initial	R076477-SCH-305	056	4092677	EDMS-PSDB-4092677	na
2/2/2005	Protocol Amendment	na	New Investigators	R092670-PSY-3004	057	4093088	EDMS-PSDB-4093088	na
2/3/2005	Safety Report	na	IN-JNJFOC-20041202092 F-2	R076477-SCH-703	058	4094614	EDMS-PSDB-4094614	na
2/4/2005	Safety Report	na	US-JNJFOC-20041100394 F-2	R076477-SCH-704	059	4098820	EDMS-PSDB-4098820	na
2/4/2005	Safety Report	na	MY-JNJFOC-20050105402 Initial	R076477-SCH-305	060	4098827	EDMS-PSDB-4098827	na
2/11/2005	Safety Report	na	RO-JNJFOC-20050201375 Initial	R076477-SCH-301	061	4115429	EDMS-PSDB-4115429	na
2/11/2005	FDA Correspondence	na	Fax: Safety Report SN 061	R076477-SCH-301	na	4140901	EDMS-PSDB-4140901	na
2/14/2005	Safety Report	na	US-JNJFOC-20050105338 F-1	R076477-SCH-305	062	4119644	EDMS-PSDB-4119644	na
2/17/2005	Safety Report	na	MY-JNJFC-20050105402 F-1	R076477-SCH-305	063	4128519	EDMS-PSDB-4128519	na
2/22/2005	Safety Report	na	RO-JNJFOC-20050201375 F-1	R076477-SCH-301	064	4137747	EDMS-PSDB-4137747	na
3/23/2005	Safety Report	na	US-JNJFOC-20050304957 Initial	R076477-SCH-1009	065	4209442	EDMS-PSDB-4209442	na
3/23/2005	General Correspondence	na	Fax: Safety Report SN 065	R076477-SCH-1009	na	4210799	EDMS-PSDB-4210799	na
3/31/2005	Safety Report	na	US-JNJFOC-20050304957 F-1	R076477-SCH-1009	066	4224908	EDMS-PSDB-4224908	na
4/4/2005	Safety Report	na	TW-JNJFOC-20050305349 Initial	R076477-SCH-305	067	4233955	EDMS-PSDB-4233955	na
4/13/2005	Safety Report	na	MY-JNJFOC-20041204460 F-1	R076477-SCH-705	068	4255811	EDMS-PSDB-4255811	na
4/15/2005	Safety Report	na	MY-JNJFOC-20041204460 F-2	R076477-SCH-705	069	4259582	EDMS-PSDB-4259582	na
4/15/2005	Safety Report	na	NL-JNJFOC-20050402753 Initial	PALIOROS-SCH-1011	070	4267510	EDMS-PSDB-4267510	na
4/15/2005	General Correspondence	na	Fax: Safety Report SN 070	PALIOROS-SCH-1011	na	4278984	EDMS-PSDB-4278984	na
4/20/2005	Safety Report	na	US-JNJFOC-20050105338 F-2	R076477-SCH-305	071	4279747	EDMS-PSDB-4279747	na
4/20/2005	Safety Report	na	MY-JNJFOC-20041105754 F-4	R076477-SCH-705	072	4279761	EDMS-PSDB-4279761	na
4/20/2005	Safety Report	na	US-JNJFOC-20041100394 F-3	R076477-SCH-704	073	4279122	EDMS-PSDB-4279122	na
4/22/2005	Safety Report	na	NL-JNJFOC-20050402753 F-1	PALIOROS-SCH-1011	074	4287661	EDMS-PSDB-4287661	na
5/9/2005	IND Amendment	na	Reclassification of IND Safety Reports	na	075	4322913	EDMS-PSDB-4322913	na
5/9/2005	Protocol Amendment	na	New Protocol: New Investigator	R092670-PSY-3003	076	4322769	EDMS-PSDB-4322769	na

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5/10/2005	Protocol Amendment	na	New Investigators	R092670-PSY-3004	077	4325611	EDMS-PSDB-4325611	na
5/11/2005	Protocol Amendment	na	New Investigators	R092670-PSY-3004	078	4329282	EDMS-PSDB-4329282	na
5/16/2005	Safety Report	na	US-JNJFOC-20050502821 Initial	R076477-SCH-1009	079	4343153	EDMS-PSDB-4343153	na
5/16/2005	FDA Correspondence	na	Fax: Safety Report SN 079	R076477-SCH-1009	na	4348879	EDMS-PSDB-4348879	na
5/23/2005	Safety Report	na	MY-JNJFOC-2004120460 F-3	R076477-SCH-705	080	4354981	EDMS-PSDB-4354981	na
5/25/2005	Safety Report	na	IN-JNJFOC-20050503897 Initial	R076477-SCH-301	081	4362170	EDMS-PSDB-4362170	na
5/25/2005	Safety Report	na	IN-JNJFOC-20050503897 F-1	R076477-SCH-301	082	4381574	EDMS-PSDB-4381574	na
6/10/2005	Information Amendment	na	CM&C	R092670-PSY-3003	083	4403047	EDMS-PSDB-1103047	na
6/13/2005	General Correspondence	na	Request for Review of Drug Product Registration Stability Protocol	na	084	4411495	EDMS-PSDB-4411495	na
6/14/2005	Information Amendment	na	Change in Protocol	R092670-PSY-3001	085	4411736	EDMS-PSDB-4411736	na
6/14/2005	Information Amendment	na	Change in Protocol	R092670-PSY-3004	086	4411745	EDMS-PSDB-4411745	na
6/15/2005	Information Amendment	na	New Protocol; New Investigators	R092670-PSY-3005	087	4416120	EDMS-PSDB-4416120	na
6/15/2005	Information Amendment	na	New Protocol; New Investigators	R092670-PSY-1001	088	4414564	EDMS-PSDB-4414564	na
6/15/2005	Safety Report	na	NL-JNJFOC-20050402753 F-2	PALIOROS-P01-1011	089	4421835	EDMS-PSDB-4421865	na
6/16/2005	Safety Report	na	US-JNJFOC-20041201617 F-1	R076477-SCH-301	090	4424386	EDMS-PSDB-4424386	na
6/17/2005	Safety Report	na	US-JNJFOC-20050103392 F-3	R076477-SCH-301	091	4431011	EDMS-PSDB-4431011	na
6/23/2005	Safety Report	na	US-JNJFOC-20050603607 Initial	R076477-SCH-705	092	4441911	EDMS-PSDB-4441911	na
6/28/2005	Protocol Amendment	na	New Protocol; New Investigators	R092670-PSY-1004	093	4460769	EDMS-PSDB-4460769	na
6/29/2005	Protocol Amendment	na	New Protocol; New Investigators	R092670-PSY-1004	094	4465586	EDMS-PSDB-4465586	na
7/11/2005	Safety Report	na	New Investigators	R076477-SCH-1009	095	4477198	EDMS-PSDB-4477198	na
7/16/2005	Safety Report	na	US-JNJFOC-20050304957 F-2	R076477-SCH-301	096	4482015	EDMS-PSDB-4482015	na
7/16/2005	Safety Report	na	US-JNJFOC-20050603607 F-1	R076477-SCH-705	097	4484198	EDMS-PSDB-4484198	na
7/19/2005	Safety Report	na	MY-JNJFOC-20041204460 F-4	R076477-SCH-705	098	4520333	EDMS-PSDB-4520333	na
7/19/2005	IND Amendment	na	Investigator's Brochure: Agenda	na	099	4525548	EDMS-PSDB-4525548	na
7/20/2005	Safety Report	na	MY-JNJFOC-20041204460 F-5	R076477-SCH-705	100	4529100	EDMS-PSDB-4529100	na
7/21/2005	Information Amendment	na	CM&C	na	101	4531527	EDMS-PSDB-4531527	na
7/26/2005	Protocol Amendment	na	New Protocol; New Investigators	R092670-PSY-1002	102	4544136	EDMS-PSDB-4544136	na
8/1/2005	IND Amendment	na	Request for Review of Revised Drug Product Registration Stability Protocol	na	103	4565568	EDMS-PSDB-4565568	na
8/5/2005	Annual Report	na	Reporting Period: 06/07/04 - 06/06/05	na	104	4574605	EDMS-PSDB-4574605	na
8/5/2005	Protocol Amendment	na	New Protocol; New Investigators	R092670-PSY-1002	105	4586146	EDMS-PSDB-4586146	na
9/9/2005	Record of Contact	na	FDA Acceptance of Amended Drug Production Registration	na	na	4692158	EDMS-PSDB-4692158	na
9/26/2005	FDA Correspondence	na	Stability Protocol for F013	R092670-PSY-3004	na	4758438	EDMS-PSDB-4758438	na
9/27/2005	Record of Contact	9/26/2005	Fax: Report to FDA from Sterling IRB Report Received from Sterling IRB Regarding CBH Health LLC	na	na	4821292	EDMS-PSDB-4821292	na
9/29/2005	General Correspondence	na	J. Martynowicz is Now Primary Contact	na	106	4762944	EDMS-PSDB-4762944	na
9/30/2005	Protocol Amendment	na	New Investigators	R092670-PSY-1004	107	4764829	EDMS-PSDB-4764829	na
9/30/2005	Protocol Amendment	na	New Investigators	R092670-PSY-3004	108	4771325	EDMS-PSDB-4771325	na
10/26/2005	Safety Report	na	RO-JNJFOC20050201375 F-2	R076477-SCH-301	109	4867147	EDMS-PSDB-4867147	na
11/11/2005	Safety Report	na	CA-JNJFOC-20051101512 Initial	R076477-SCH-705	110	4925304	EDMS-PSDB-4925304	na
11/21/2005	Safety Report	na	CA-JNJFOC-20051101512 F-1	R076477-SCH-705	111	4951293	EDMS-PSDB-4951293	na
11/29/2005	IND Amendment	na	Request for Review of Revised Drug Product Registration Stability Protocol	na	112	4966845	EDMS-PSDB-4966845	na
12/20/2005	Record of Contact	12/7/2005	Minutes of the 12/7/05 Bipolar I Disorder End-of-Phase 2/Pre-Phase 3 Meeting	na	na	5019672	EDMS-PSDB-5019672	na
12/21/2005	General Correspondence	na	Minutes of the 12/7/05 End of Phase 2 Meeting	na	113	5029714	EDMS-PSDB-5029714	na
12/22/2005	Safety Report	na	CA-JNJFOC-20051101512 F-2	R076477-SCH-705	114	5030729	EDMS-PSDB-5030729	na
12/29/2005	Safety Report	na	CA-JNJFOC-20051101512 F-3	R076477-SCH-705	115	5040289	EDMS-PSDB-5040289	na
2/2/2006	Protocol Amendment	na	New Protocol; New Investigators	R092670-PSY-3002	116	5131076	EDMS-PSDB-5131076	na
2/23/2006	Protocol Amendment	na	New Investigators	R092670-PSY-3004	117	5205422	EDMS-PSDB-5205422	na

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3/6/2006	General Correspondence	na	IRB Waiver Request	na	118	5248420	EDMS-PSDB-5248420	na
3/24/2006	Safety Report	na	IN-JNJFOC-20060205306 7/15 Day Initial	R076477-SCH-701	119	5324478	EDMS-PSDB-5324478	na
3/24/2006	General Correspondence	na	Fax: IN-JNJFOC-20060205306 7/15 Day Initial	R076477-SCH-701	119	5358805	EDMS-PSDB-5358805	na
3/27/2006	Information Amendment	na	Clinical: Statistical Analysis Plan for R092670-PSY-3004	R092670-PSY-3004	120	5330146	EDMS-PSDB-5330146	na
4/3/2006	General Correspondence	na	Fax: IN-JNJFOC-20060205306 7/15 Day F-1	R076477-SCH-701	121	5352966	EDMS-PSDB-5352966	na
5/26/2006	FDA Correspondence	na	Letter: IRB Waiver Request Granted (S-117)	R092670-PSY-3004	na	5546925	EDMS-PSDB-5546925	na
5/26/2006	FDA Correspondence	na	Email/Attachment: IRB Waiver Request Granted (S-117)	R092670-PSY-3004	na	5545009	EDMS-PSDB-5545009	na
6/20/2006	IND Amendment	na	Protocol R092670-PSY-3003 Medication Kit Error	R092670-PSY-3003	122	5593354	EDMS-PSDB-5593354	na
6/26/2006	Information Amendment	na	Clinical: Statistical Analysis Plan for R092670-PSY-3003	R092670-PSY-3003	123	5617192	EDMS-PSDB-5617192	na
6/27/2006	Record of Contact	6/23/2006	DSI Notification of Study Compliance Deficiencies	na	na	6380254	EDMS-PSDB-6380254	na
7/11/2006	Information Amendment	na	Clinical	R092670-PSY-3001; R092670-PSY-3002; R092670-PSY-1004	124	5645851	EDMS-PSDB-5645851	na
7/12/2006	Safety Report	na	IN-JNJFOC-20060205306 F-2	R076477-SCH-701	125	5662755	EDMS-PSDB-5662755	na
7/17/2006	FDA Correspondence	na	Email/Attachment: Poland Investigator Site Audit with CL for SN 124	R092670-PSY-3001; R092670-PSY-3002; R092670-PSY-1004	na	5704533	EDMS-PSDB-5704533	na
7/21/2006	FDA Correspondence	na	Email: SAP for R092670-PSY-3003	R092670-PSY-3003	na	5714883	EDMS-PSDB-5714883	na
7/31/2006	FDA Correspondence	na	Email: FDA Response to Statistical Questions from 6/26/06	na	na	6033820	EDMS-PSDB-6033820	na
8/10/2006	IND Amendment	na	Investigator's Brochure: Addendum	na	126	5755623	EDMS-PSDB-5755623	na
8/14/2006	IND Amendment	na	Gen Corr: Request for Type B Pre-Phase 3 Meeting	na	127	5765064	EDMS-PSDB-5765064	na
8/17/2006	FDA Correspondence	na	Email: Secure E-Mail	na	na	5799979	EDMS-PSDB-5799979	na
9/1/2006	IND Amendment	na	Gen Corr: Request for Type C Meeting	na	128	5827016	EDMS-PSDB-5827016	na
9/6/2006	Safety Report	na	IN-JNJFOC-20060805629 Initial	R076477-BIM-3002	129	5836723	EDMS-PSDB-5836723	na
9/12/2006	FDA Correspondence	na	Email/Attachment: Meeting Request	na	na	5922314	EDMS-PSDB-5922314	na
9/18/2006	Annual Report	na	Reporting Period: 06/07/05 - 06/06/06	na	130	5868840	EDMS-PSDB-5868840	na
9/20/2006	FDA Correspondence	na	Email: Electronic Submissions	na	na	5922383	EDMS-PSDB-5922383	na
9/21/2006	General Correspondence	na	Request for Special Protocol Assessment	R076477-SCA-3003	131	5895887	EDMS-PSDB-5895887	na
9/22/2006	FDA Correspondence	na	Email: Meeting Granted	na	na	5922505	EDMS-PSDB-5922505	na
9/22/2006	FDA Correspondence	na	Email: Bipolar & Schizophrenia Meeting Requests	na	na	5922449	EDMS-PSDB-5922449	na
9/25/2006	FDA Correspondence	na	Email: Bipolar & Schizophrenia Meeting Requests	na	na	5922559	EDMS-PSDB-5922559	na
9/26/2006	FDA Correspondence	na	Email: Meeting Granted (12:08pm)	na	na	5922643	EDMS-PSDB-5922643	na
9/26/2006	FDA Correspondence	na	Email: Meeting Granted (3:22pm)	na	na	5922614	EDMS-PSDB-5922614	na
9/26/2006	Safety Report	na	IN-JNJFOC-20060805629 F-1	R076477-BIM-3002	132	5908836	EDMS-PSDB-5908836	na
10/6/2006	General Correspondence	na	eCTD Submission Conversion	na	133	0000	GW eCTD TOC	na
10/11/2006	Safety Report	na	IN-JNJFOC-20060205306 7/15 Day F-3	R076477-SCH-701	134	0134	GW eCTD TOC	na
10/18/2006	Safety Report	na	IN-JNJFOC-20060805629 F-2	R076477-BIM-3002	135	0135	GW eCTD TOC	na
10/27/2006	FDA Correspondence	na	Email: Transfer of Regulatory Responsibility	na	na	6027759	EDMS-PSDB-6027759	na
11/3/2006	FDA Correspondence	na	Letter: RFI in Response to 9/21/06 Request for Special Protocol Assessment	na	na	6058010	EDMS-PSDB-6058010	na
11/6/2006	Information Amendment	na	Clinical: Statistical Analysis Plan for PSY-3001	R092670-PSY-3001	136	0136	GW eCTD TOC	na
11/9/2006	General Correspondence	na	Briefing Pkg. For 12/11/06 Type C Meeting	na	137	0137	GW eCTD TOC	na
11/27/2006	Safety Report	na	IN-JNJFOC-20060805629 F-3	R076477-BIM-3002	138	0138	GW eCTD TOC	na
12/4/2006	FDA Correspondence	na	Email: N136 Stats Comments	na	na	6159463	EDMS-PSDB-6159463	na
12/7/2006	FDA Correspondence	na	Email/Attachment: N136 Stats Comments	R092670-PSY-3001	na	6163931	EDMS-PSDB-6163931	na
12/8/2006	Safety Report	na	SE-JNJFOC-20061005337 I	R092670-PSY-3002	139	0139	GW eCTD TOC	na
12/18/2006	Safety Report	na	Multiple (9)	Multiple	140	0140	GW eCTD TOC	na
12/18/2006	Safety Report	na	DE-JNJFOC-20061200532 I	R076477-BIM-3004	141	0141	GW eCTD TOC	na
12/19/2006	Information Amendment	na	Clinical: Statistical Analysis Plan for R092670-PSY-3001	R092670-PSY-3001	142	0142	GW eCTD TOC	na
12/21/2006	Record of Contact	12/11/2006	Minutes from the Meeting with the FDA Division of Psychiatry Products on 12/11/06	na	na	6218032	EDMS-PSDB-6218032	na
12/22/2006	Protocol Amendment	na	Statistical Analysis Plan for R092670-PSY-3005	R092670-PSY-3005	143	0143	GW eCTD TOC	na

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Date	Submission Type	Date of Contact	Description	Protocol #	SN#	EDMS or Sequence #	Hyperlink	Gateway Receipt
12/27/2006	IND Amendment	na	Minutes of December 11, 2006 Type C Meeting	na	144	0144	GW eCTD TOC	na
12/29/2006	FDA Correspondence	na	Letter: Official Meeting Minutes from 12/11/06 Telecon	na	na	6248267	EDMS-PSDB-6248267	na
1/3/2007	FDA Correspondence	na	Email/Attachment: Official Meeting Minutes from 12/11/06 Telecon	na	na	6241885	EDMS-PSDB-6241885	na
1/4/2007	Protocol Amendment	na	New Protocol	R092670-PSY-3007	145	0145	GW eCTD TOC	na
1/9/2007	General Correspondence	na	Request for Type B Pre-Phase 3 Meeting	na	146	0146	GW eCTD TOC	na
1/9/2007	FDA Correspondence	na	Email/Attachment: Meeting Request, Paliperidone Palmitate Bipolar Development Program	na	na	6264901	EDMS-PSDB-6264901	na
1/19/2007	FDA Correspondence	na	Email: Plan to Stop Study R092670-PSY-3001	R092670-PSY-3001	na	6308521	EDMS-PSDB-6308521	na
1/23/2007	Record of Contact	na	FDA Div. Of Scientific Affairs: Telephone Contact Memo: Between FDA and Local Trial Manager in Global Clinical Operations	R092670-PSY-3001	na	6360613	EDMS-PSDB-6360613	na
1/24/2007	General Correspondence	na	Response to RFI: Copy of Protocol R092670-PSY-3001	R092670-PSY-3001	na	6324934	EDMS-PSDB-6324934	na
1/26/2007	Protocol Amendment	na	Notification of PSY-3001 Study Termination Due to Efficacy, Change in Protocol R092670-PSY-3001; Final Statistical Analysis Plan for R092670-PSY-3001	R092670-PSY-3001	147	0147	GW eCTD TOC	na
1/31/2007	General Correspondence	na	IRB Waiver Request	R092670-PSY-3007	148	0148	GW eCTD TOC	na
2/2/2007	Protocol Amendment	na	New Protocol: New Investigators	R092670-PSY-3006	149	0149	GW eCTD TOC	na
2/6/2007	IND Amendment	na	IRB Waiver Request	R092670-PSY-3006	150	0150	GW eCTD TOC	na
2/11/2007	Record of Contact	2/6/2007	GCP Violations at Dr. Chaganiti's Site Under Protocol R092670-PSY-3001	R092670-PSY-3001	na	6383191	EDMS-PSDB-6383191	na
2/12/2007	General Correspondence	na	Response to RFI from DSI: Protocol R092670-PSY-3001	R092670-PSY-3001	151	0151	GW eCTD TOC	na
2/15/2007	Safety Report	na	Site Closure: MedClin Research, Inc.	R076477-SCA-3002	152	0152	GW eCTD TOC	na
2/16/2007	General Correspondence	na	US-JNJFOC-20070201813 Initial	na	153	0153	GW eCTD TOC	na
2/16/2007	FDA Correspondence	na	Request for a Type B, Pre-NDA Meeting	na	154	6416129	EDMS-PSDB-6416129	na
2/16/2007	FDA Correspondence	na	Fax/Attachment: 7/15 Day Safety Report (K.Kiedrow)	na	154	6415933	EDMS-PSDB-6415933	na
2/16/2007	Safety Report	na	Fax/Attachment: 7/15 Day Safety Report (D.Bates)	na	154	154	GW eCTD TOC	na
2/22/2007	FDA Correspondence	na	US-JNJFOC-20070203055 Initial 7/15 Day Report	R076477-BIM-3004	na	6429676	EDMS-PSDB-6429676	na
2/22/2007	Safety Report	na	Email: 4/18/07 Type B Meeting Request Granted	na	na	0155	GW eCTD TOC	na
2/26/2007	Safety Report	na	US-JNJFOC-20070204832 Initial	R076477-SCA-3001	155	6446121	EDMS-PSDB-6446121	na
2/26/2007	Safety Report	na	Fax: US-JNJFOC-20070204832 Initial	R076477-SCA-3001	155	6452312	EDMS-PSDB-6452312	na
2/26/2007	FDA Correspondence	na	Letter: IRB Waiver Granted for 2/6/07 SN 150 Submission	R092670-PSY-3006	na	6526103	EDMS-PSDB-6526103	na
2/26/2007	FDA Correspondence	na	Letter: IRB Waiver Granted for 1/31/07 SN 148 Submission	R092670-PSY-3007	na	0156	GW eCTD TOC	na
2/28/2007	Safety Report	na	US-JNJFOC-20070203055 F-1	R076477-BIM-3004	156	0157	GW eCTD TOC	na
3/5/2007	Safety Report	na	US-JNJFOC-20070204832 F-1	R076477-SCA-3001	157	0158	GW eCTD TOC	na
3/6/2007	Protocol Amendment	na	New Investigator	R092670-PSY-3007	158	0159	GW eCTD TOC	na
3/9/2007	Protocol Amendment	na	New Investigator	R092670-PSY-3006	159	0160	GW eCTD TOC	na
3/15/2007	IND Amendment	na	Briefing Package for 4/18/07 Type B Pre-NDA Meeting	na	160	0161	GW eCTD TOC	na
3/20/2007	Safety Report	na	US-JNJFOC-20070204832 F-2	R076477-SCA-3001	161	0162	GW eCTD TOC	na
3/22/2007	Protocol Amendment	na	Change in Protocol and Statistical Analysis Plan	R092670-PSY-3002	162	0163	GW eCTD TOC	na
3/26/2007	General Correspondence	na	Request for a Type B CMC/BioPharmaceutics Pre-NDA Meeting	na	163	0164	GW eCTD TOC	na
3/28/2007	Information Amendment	na	Clinical	na	164	0165	GW eCTD TOC	na
3/30/2007	Protocol Amendment	na	New and Updated Investigators	R092670-PSY-3007	165	6614450	EDMS-PSDB-6614450	na
3/30/2007	FDA Correspondence	na	Email: Request for Submission Information	na	na	6637219	EDMS-PSDB-6637219	na
4/5/2007	FDA Correspondence	na	Email: SN 162 SAP - Question about Submission Study	R092670-PSY-3002	na	0166	GW eCTD TOC	na
4/6/2007	General Correspondence	na	Response to FDA RFI: Additional Safety Information	na	166	6637270	EDMS-PSDB-6637270	na
4/9/2007	FDA Correspondence	na	Email: Reply to FDS's 4/5/07 Study Question	R092670-PSY-3002	na	na	04-11-07 Email	na
4/11/007	FDA Correspondence	na	Email: S/162 SAP	na	na	0167	GW eCTD TOC	na
4/16/2007	Safety Report	na	RO-JNJFOC-20060503643 F-1	R092670-PSY-3001	167	0168	GW eCTD TOC	na
4/17/2007	Safety Report	na	US-JNJFOC-20070203055 F-2	R076477-BIM-3004	168	0169	GW eCTD TOC	na
4/19/2007	Safety Report	na	US-JNJFOC-20070401462 Initial	R076477-BIM-3002	169	0169	GW eCTD TOC	na

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Date	Submission Type	Date of Contact	Description	Protocol #	SN#	EDMS or Sequence #	Hyperlink	Gateway Receipt
4/24/2007	FDA Correspondence	na	Email: Meeting Granted & Request for Meeting Pkg. By 5/10/07 S/163	na	na	6733756	EDMS-PSDB-6733756	na
4/25/2007	Safety Report	na	DE-JNJFOC-20061200532 F-1	R076477-BIM-3004	170	0170	GW eCTD TOC	na
4/30/2007	Safety Report	na	US-JNJFOC-20070405377 7-Day Initial	R076477-BIM-3004	171	0171	GW eCTD TOC	na
4/30/2007	FDA Correspondence	na	Fax: SN 171	na	na	6793658	EDMS-PSDB-6793658	na
4/30/2007	FDA Correspondence	na	Fax: SN 171 (2nd sending of fax)	na	na	6793660	EDMS-PSDB-6793660	na
5/3/2007	FDA Correspondence	na	Letter: 04/18/07 Official Meeting Minutes S/153	na	na	6801969	EDMS-PSDB-6801969	na
5/3/2007	FDA Correspondence	na	US-JNJFOC-20070405377 7-Day F-1	R076477-BIM-3004	172	0172	GW eCTD TOC	na
5/4/2007	Safety Report	na	US-JNJFOC-20070404476 Initial	R076477-BIM-3001	173	0173	GW eCTD TOC	na
5/4/2007	Safety Report	na	US-JNJFOC-20070405377 7-Day F-2	R076477-BIM-3004	174	0174	GW eCTD TOC	na
5/7/2007	Safety Report	na	US-JNJFOC-20070404476 F-1	R076477-BIM-3001	175	0175	GW eCTD TOC	na
5/8/2007	Safety Report	na	Email/Attachment: 04/18/07 Meeting Minutes S/153	na	na	6806260	EDMS-PSDB-6806260	na
5/7/2007	FDA Correspondence	na	Briefing Package for 6/7/07 CMC/BioPharmaceutics Type B pre-NDA Meeting	na	176	0176	GW eCTD TOC	na
5/9/2007	Safety Report	na	US-JNJFOC-20070204832 F-3	R076477-SCA-3001	177	0177	GW eCTD TOC	na
5/9/2007	FDA Correspondence	na	Letter: 1/4/07 SN 145 Statistical Review with Comments	R092670-PSY-3007	na	na	05-09-07 Letter	na
5/11/2007	General Correspondence	na	Minutes of the 4/18/07 Pre-NDA Meeting	na	178	0178	GW eCTD TOC	na
5/16/2007	Safety Report	na	US-JNJFOC-20070201813 F-1	R076477-SCA-3002	179	0179	GW eCTD TOC	na
5/22/2007	Safety Report	na	US-JNJFOC-20070204832 F-4	R076477-SCA-3001	180	0180	GW eCTD TOC	na
5/24/2007	Protocol Amendment	na	Change in Protocol; New Investigators	R092670-PSY-3006	181	0181	GW eCTD TOC	na
5/25/2007	Information Amendment	na	Nonclinical Pharmacology Study Report	na	182	0182	GW eCTD TOC	na
6/4/2007	FDA Correspondence	na	Email/Attachment: Preliminary Comments for 6/7/07 Meeting	na	na	na	06-04-07 Email	na
6/8/2007	Record of Contact	6/8/2007	Protocol PSY-3001 "Rater" Qualifications	R092670-PSY-3001	na	6963412	EDMS-PSDB-6963412	na
6/8/2007	Protocol Amendment	na	Change in Protocol; New Investigators	R092670-PSY-3007	183	0183	GW eCTD TOC	na
6/14/2007	Protocol Amendment	na	New Protocol	R092670-PSY-1008	184	0184	GW eCTD TOC	na
6/15/2007	General Correspondence	na	IRB Waiver Request	R092670-PSY-1008	185	0185	GW eCTD TOC	na
6/15/2007	FDA Correspondence	na	Email: IND 67,356 3-Month Product Formulation: IND 76,952	na	na	na	06-15-07 Email	na
6/29/2007	FDA Correspondence	na	Letter: 06/07/07 Official Meeting Minutes	R092670-PSY-3006	186	0186	GW eSIG TOC	na
7/31/2007	Protocol Amendment	na	Change in Protocol	R092670-PSY-3007	187	0187	GW eSIG TOC	na
8/1/2007	Protocol Amendment	na	New Investigators	na	188	0188	GW eSIG TOC	na
8/13/2007	General Correspondence	na	Clarification of Official Minutes of the 07 June 2007 Meeting - CMC & BioPharmaceutics pre-NDA	na	na	na	na	na
8/21/2007	Safety Report	na	DE-JNJFOC-20061200532 F-2	R076477-BIM-3004	189	0189	GW eSIG TOC	na
8/27/2007	General Correspondence	na	Sample Dataset Submission for IT Testing	na	190	0190	GW eSIG TOC	na
9/12/2007	FDA Correspondence	na	Email: Paliperidone palmitate NDA Submission Plans	na	na	na	09-12-07 Email	na
9/19/2007	Protocol Amendment	na	Change in Protocol; New Investigators	R092670-PSY-1008	191	0191	GW eSIG TOC	na
9/20/2007	Annual Report	na	Reporting Period: 07/20/06 - 07/19/07	na	192	0192	GW eSIG TOC	na
11/1/2007	Protocol Amendment	na	New Investigators	R092670-PSY-3007	193	0193	GW eSIG TOC	na
11/2/2007	Protocol Amendment	na	New Investigators	R092670-PSY-3006	194	0194	GW eSIG TOC	na
11/29/2007	Safety Report	na	DE-JNJFOC-20061200532 F-3	R076477-BIM-3004	195	0195	GW eSIG TOC	na
12/6/2007	Record of Contact	6/16/2004	Minutes of June 16, 2004 CMC/BioPharmaceutics End of Phase 2 Meeting for Paliperidone Palmitate	na	na	na	12-06-07 Email	na
12/11/2007	Information Amendment	na	CMC Drug Substance, Drug Product and Stability Data	na	196	0196	GW eSIG TOC	na
12/21/2007	General Correspondence	na	Request for Proposed Proprietary Name Review	na	197	0197	GW eSIG TOC	na
12/27/2007	Protocol Amendment	na	New Investigators	R092670-PSY-3006	198	0198	GW eSIG TOC	na
1/9/2008	Information Amendment	na	Pharmacology/Toxicology	na	199	0199	GW eSIG TOC	na
1/15/2008	Protocol Amendment	na	New Investigators	R092670-PSY-3007	200	0200	GW eSIG TOC	na
1/23/2008	Protocol Amendment	na	Statistical Analysis Plan for R092670-PSY-3007	R092670-PSY-3007	201	0201	GW eSIG TOC	na
1/25/2008	General Correspondence	na	Postmarketing Study Commitment Final Report: Developmental Toxicity Study in the Rat Final Report	na	202	0202	GW eSIG TOC	na
1/30/2008	FDA Correspondence	na	Email/Attachment: IRB Waiver Granted	na	na	na	01-30-08 Email	na
2/1/2008	Protocol Amendment	na	New Investigators	R092670-PSY-1008	203	0203	GW eSIG TOC	na

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Date	Submission Type	Date of Contact	Description	Supply	EDMS or Sequence #	Hyperlink	Gateway Receipt
10/25/2007	Original NDA	na	Original New Drug Application	na	0000	GW eSIG TOC	na
10/26/2007	General Correspondence	na	Desk Copy - Review Aid	na	na	10-26-07 Desk Copy	na
11/7/2007	FDA Correspondence	na	Letter: NDA Receipt Acknowledgement	na	na	11-07-07 Letter	na
12/5/2007	FDA Correspondence	na	Email: Information Request	na	na	12-05-07 Email	na
12/7/2007	FDA Correspondence	na	Email/Attachment: Request for Datasets	na	na	12-07-07 Email	na
12/11/2007	NDA Amendment	na	Response to FDA Request for Carcinogenicity Tumor Dataset	na	0001	GW eSIG TOC	na
12/19/2008	FDA Correspondence	na	Email: 3-Month Pali Palmitate IND 76,952 Plans and NDA 22-264 Tradename Question	na	na	12-19-07 Email	na
12/21/2007	General Correspondence	na	Request for Proposed Proprietary Name Review	na	0002	GW eSIG TOC	na
12/21/2007	FDA Correspondence	na	Email/Attachment: Filing Communication Letter	na	na	12-21-07 Email	na
12/21/2007	FDA Correspondence	na	Letter: Filing Communication Letter	na	na	12-21-07 Letter	na
1/9/2008	General Correspondence	na	Response to FDA Filing Communication: Request for Carcinogenicity Data Variables	na	0003	GW eSIG TOC	na
1/10/2008	FDA Correspondence	na	Email/Attachment: Reformatted Tumor Dataset	na	na	01-10-08 Email	na
1/30/2008	FDA Correspondence	na	Email/Attachment: Review of the NDA	na	na	01-30-08 Email	na
2/7/2008	FDA Correspondence	na	Email: Dystonia Class Labeling Follow-up to Our Earlier Discussion	na	na	02-07-08 Email	na
2/11/2008	FDA Correspondence	na	Email/Attachment: RISPERDAL and INVEGA Clinical Development Program Analyses	na	na	02-11-08 Email	na
2/25/2008	Safety Update	na	4-Month Safety Update	na	0004	GW eSIG TOC	na
2/27/2008	General Correspondence	na	Response to FDA RFI: SAS Data Sets for Study R092670-PSY-3001	na	0005	GW eSIG TOC	na
2/28/2008	FDA Correspondence	na	Email/Attachments: 4-Month Safety Update-Response to Email Dated 14 Feb for SAS Data Sets	na	na	02-25-08 Email	na
2/27/2008	General Correspondence	na	Transfer of NDA Ownership	na	0006	GW eSIG TOC	na
2/27/2008	General Correspondence	na	Transfer of NDA Ownership	na	0007	GW eSIG TOC	na
3/21/2008	FDA Correspondence	na	Email/Attachment: Metabolic Parameter Request	na	na	03-21-08 Email	na
4/9/2008	FDA Correspondence	na	Email: Voice Mail Follow-up: Study R092670-PSY-3001	na	na	04-09-08 Email	na
4/22/2008	FDA Correspondence	na	Letter: Request for CMC Information	na	na	04-22-08 Letter	na
4/30/2008	FDA Correspondence	na	Email: CMC Questions	na	na	04-30-08 Email	na
5/2/2008	General Correspondence	na	Response to FDA RFI: Study Center Information	na	0008	GW eSIG TOC	na
5/12/2008	FDA Correspondence	na	Email: Request for Update on Information Request Response	na	na	05-12-08 Email	na
5/12/2008	General Correspondence	na	Response to FDA RFI: IVVC Information	na	0009	GW eSIG TOC	na
5/13/2008	FDA Correspondence	na	Email: Follow-up Information on Study R076477-PSY-3001	na	na	05-13-08 Email	na
5/16/2008	FDA Correspondence	na	Email: Biopharmaceutics Telecon	na	na	05-16-08 Email	na
5/18/2008	FDA Correspondence	na	Email: CMC Response Timeline	na	na	05-18-08 Email	na
5/20/2008	FDA Correspondence	na	Letter: Comments Re: CMC Section of 10/25/07 Submission	na	na	05-20-08 Letter	na
5/21/2008	General Correspondence	na	Status of Ongoing Study R076477-PSY-3001, Pending NDA 22-264	na	0010	GW eSIG TOC	na
5/21/2008	General Correspondence	na	Desk Copy - Review Aid	na	na	05-21-08 Desk Copy	na
5/22/2008	FDA Correspondence	na	Email/Attachment: Biopharm Teleconference on 19 May 2008	na	na	05-22-08 Email	na
5/23/2008	FDA Correspondence	na	Email/Attachment: Biopharm Teleconference on 19 May 2008	na	na	05-23-08 Email	na
5/23/2008	FDA Correspondence	na	Email: Information Request	na	na	05-23-08 Email	na
5/27/2008	FDA Correspondence	na	Email: Receipt of Questions	na	na	05-27-08 Email	na
5/28/2008	General Correspondence	na	Minutes of 19 May 2008 Teleconference	na	0011	GW eSIG TOC	na
5/28/2008	General Correspondence	na	Response to FDA RFI: CMC Request of 22 April 2008	na	0012	GW eSIG TOC	na
6/2/2008	General Correspondence	na	Response to FDA RFI: Adverse Event Rates and Revised Table 1	na	0013	GW eSIG TOC	na
6/3/2008	General Correspondence	na	Response to FDA RFI: IVVC Supporting Data and Computer Programs	na	0014	GW eSIG TOC	na
6/3/2008	FDA Correspondence	na	Email: FDA Request for Samples of Pali Palmitate Drug Product	na	na	06-03-08 Email	na

2/3/2009	General Correspondence	na	Resubmission: Sponsor's Responses to FDA's Complete Response Letter	na	0026	GW eSIG TOC	22264-0026_eSIG
2/6/2009	FDA Correspondence	na	Email from FDA: Tradename Submission	na	na	02-06-09 Email	na
2/11/2009	Other	na	Request for Proprietary Name Review: Re-review of Previous Tentatively Approved Proprietary Name	na	0027	GW eSIG TOC	22264-0027_eSIG
2/13/2009	FDA Correspondence	na	Email/Attachment from FDA: 2/2/09 Submission is a Class 2 Resubmission with a 6 Month Review Cycle	na	na	02-13-09 Email	na
2/13/2009	FDA Correspondence	na	FDA Letter: 02/03/09 Submission Receipt Acknowledgement	na	na	02-13-09 Letter	na
2/24/2009	General Correspondence	na	Response to Request for Information: CMC Drug Substance	na	0028	GW eSIG TOC	22264-0028_eSIG
3/24/2009	Other	na	Certification for Delay of Posting Clinical Trial Results on www.ClinicalTrials.gov	na	0029	GW eCTD TOC	22264-0029_eSIG
3/30/2009	FDA Correspondence	na	Email from FDA: RFI - DMF 20902 Vacuum Leak Test Method	na	na	03-30-09 Email	na
4/3/2009	FDA Correspondence	na	Email/Attachments to FDA: DMF 20902 Response to Request from 03/30/09	na	na	04-03-09 Email	na
4/24/2009	FDA Correspondence	na	FDA Letter: CMC Reviewer RFI	na	na	04-24-09 Letter	na
5/1/2009	FDA Correspondence	na	Email from FDA: DMF 20902 Amendment - Additional Stability Data Included for Cork	na	na	05-01-09 Email	na
5/5/2009	FDA Correspondence	na	Email from FDA: Review Team RFI - "Mock-up" Copy of Proposed Syringe and Carton Kit	na	na	05-05-09 Email	na
5/7/2009	General Correspondence	na	Pre-Launch Activities Importation Request	na	0030	GW eSIG TOC	22264-0030_eSIG
5/8/2009	FDA Correspondence	na	Email/Attachments to FDA: Pre-Launch Activities Importation Request	na	na	05-08-09 Email	na
5/14/2009	FDA Correspondence	na	Email to FDA: Mock-ups of INVEGA SUSTENNA Commercial Product	na	na	05-14-09 Email	na
5/15/2009	General Correspondence	na	Response to RFI: Clinical Study Report PALIROS-PSZ-1001	na	0031	GW eSIG TOC	22264-0031_eSIG
5/15/2009	FDA Correspondence	na	Email to FDA: Information Request	na	na	05-15-09 Email	na
5/15/2009	FDA Correspondence	na	FDA Letter: Proposed Proprietary Name, INVEGA SUSTENNA, Acceptable	na	na	05-15-09 Letter	na
5/18/2009	FDA Correspondence	na	Email/Attachment to FDA: Information Request - Xu et al Publication	na	na	05-18-09 Email	na
5/20/2009	General Correspondence	na	Response to RFI: Efficacy Subgroup Analyses for R092670-PSV-3007	na	0032	GW eSIG TOC	22264-0032_eSIG
5/20/2009	FDA Correspondence	na	Email/Attachments: Information Request	na	na	05-20-09 Email	na
5/22/2009	General Correspondence	na	Response to RFI: CM&C Response to Information Request Letter of 23 April 2009	na	0033	GW eSIG TOC	22264-0033_eSIG
5/25/2009	General Correspondence	na	Response to RFI: SAS Programs for PSP Analyses	na	na	05-25-09 Gen Corr	na
5/26/2009	FDA Correspondence	na	Email/Attachment to FDA: SAS Code for PSP Analyses - Information Request for NDA 22-264	na	na	05-26-09 Email	na
5/27/2009	FDA Correspondence	na	Email to FDA: Mock-ups - RE: SAS Code for PSP Analysis - Information Request for NDA 22-264	na	na	05-27-09 Email	na
6/1/2009	FDA Correspondence	na	Email from FDA: Request for Information - Liver Enzymes	na	na	06-01-09 Email	na
6/4/2009	FDA Correspondence	na	Email from FDA: Information Request for Additional Financial Disclosure Information	na	na	06-04-09 Email	na
6/5/2009	FDA Correspondence	na	Email/Attachment to FDA: Response to Request for Location of Narratives for Elevated Liver Enzymes	na	na	06-05-09 Email	na
6/8/2009	FDA Correspondence	na	Email/Attachments to FDA: Janssen Pharmaceutica N.V. Samples to FDA	na	na	06-08-09 Email	na
6/8/2009	FDA Correspondence	na	Email from FDA: Re: Janssen Pharmaceutica N.V. Samples to FDA	na	na	06-08-09 Email	na
6/9/2009	Other	na	Pre-Launch Activities Importation Request Amendment	na	0034	GW eSIG TOC	22264-0034_eSIG
6/11/2009	FDA Correspondence	na	Email/Attachment to FDA: UPS Tracking Numbers for Samples	na	na	06-11-09 Email	na
6/15/2009	FDA Correspondence	na	Email from FDA: Information Request (Simulation Code and Dataset)	na	na	06-15-09 Email	na
6/15/2009	FDA Correspondence	na	Email to FDA: Information Request (Simulation Code and Dataset)	na	na	06-15-09 Email	na
6/16/2009	FDA Correspondence	na	Email from FDA: Information Request (Simulation Code and Dataset)	na	na	06-16-09 Email	na

